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 IV

Donald P. Francis, M.D., D.Sc.	EPIDEMIOLOGIST, CENTERS FOR DISEASE CONTROL: DEFINING AIDS AND ISOLATING THE HUMAN IMMUNODEFICIENCY VIRUS (HIV)
Merle A. Sande, M.D.	INFECTIOUS DISEASE SPECIALIST: AIDS TREATMENT AND INFECTION CONTROL AT SAN FRANCISCO GENERAL HOSPITAL
John L. Ziegler, M.D., Ph.D.	ONCOLOGIST: KAPOSI'S SARCOMA AND AIDS RESEARCH IN SAN FRANCISCO AND GLOBALLY

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

Interviews Conducted by
Sally Smith Hughes
in 1993 and 1994

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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Donald P. Francis, M.D., D.Sc. (b. 1942), epidemiologist, Centers for Disease Control (CDC), 1971-1989: early research with the Ebola virus; first reports of the AIDS epidemic; defining AIDS; risk groups for AIDS; politics and the CDC; isolating the human immunodeficiency virus (HIV); blood screening and blood safety issues; civil rights versus public health.
Merle A. Sande, M.D. (b. 1939), infectious disease specialist; professor of medicine, UC San Francisco (UCSF), and chief of medical services, San Francisco General Hospital (SFGH), 1980-1996: infection control concerns; guidelines for AIDS health workers; UCSF Task Force on AIDS; the AIDS outpatient clinic and inpatient ward at SFGH; AIDS treatment; physician-patient relationship; AIDS Clinical Research Forum; the San Francisco model of AIDS care.
John L. Ziegler, M.D., Ph.D. (b. 1938) oncologist; chief of staff, Veterans Administration Medical Center and UCSF professor of medicine: Kaposi's sarcoma in gay men (early cases); the Kaposi's Sarcoma Study Group; the etiology of Kaposi's sarcoma; founding the AIDS Clinical Research Center(s); the Kaposi's Sarcoma Clinic at UCSF; AIDS research activities and funding; treating AIDS-related lymphomas and opportunistic infections; recognizing a global epidemic; theories of etiology of AIDS and of Kaposi's sarcoma.

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

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

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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.

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September 1994
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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 AIDS MEDICAL RESPONSE 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

VOLUME IV

Donald P. Francis, M.D., D.Sc., Epidemiology and Virology at the Centers for Disease Control
Merle A. Sande, M.D., Infectious Disease Specialist; Professor of Medicine, UCSF-SFGH; AIDS Activities at San Francisco General Hospital
John L. Ziegler, M.D., Ph.D., Professor of Medicine, UCSF; AIDS Oncologist at the Veterans Administration Medical Center, San Francisco

IN PROCESS

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 (On Hold)
Herbert C. Perkins, M.D., President, Irwin Memorial Blood Centers
Warren Winkelstein, Jr., M.D., M.P.H., The San Francisco Men's Health Study, UC Berkeley

Regional Oral History Office
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University of California
Berkeley, California

The San Francisco AIDS Oral History Series

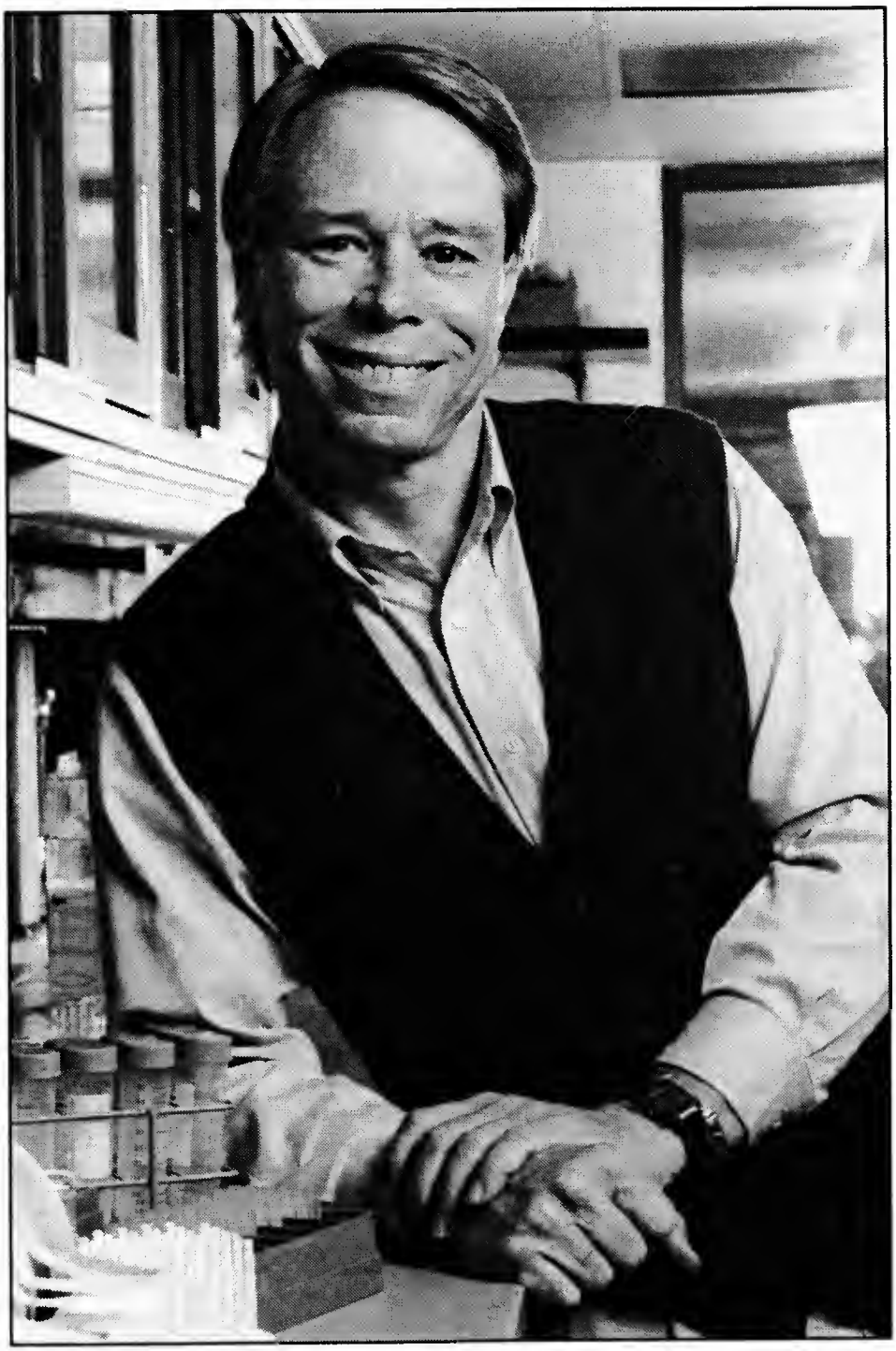
THE AIDS EPIDEMIC IN SAN FRANCISCO: THE MEDICAL RESPONSE, 1981-1984

Volume IV

Donald P. Francis, M.D., D.Sc.

EPIDEMIOLOGIST, CENTERS FOR DISEASE CONTROL: DEFINING AIDS AND ISOLATING THE HUMAN IMMUNODEFICIENCY VIRUS (HIV)

Interviews Conducted by
Sally Smith Hughes
in 1993 and 1994



Donald P. Francis, ca. 1994.

Interview History--by Sally Smith Hughes, Ph.D.

Thanks partly to Randy Shilts' book, And the Band Played On, and the film based on it, Donald Francis is one of the most visible figures in AIDS science and politics. In the oral history, the reader will learn of his efforts in the 1970s as an Epidemic Intelligence Service Officer of the Centers for Disease Control [CDC] to stamp out disease in exotic areas of the world, including smallpox and Ebola fever in Sudan. He then tells of his doctoral research in Max Essex's group at the Harvard School of Public Health on feline leukemia, an immunodeficiency disease caused by a retrovirus. This work "prepared" him in unexpected ways to deal with the epidemic of immunodeficiency disease in gay men reported in 1981, less than two years after he had received a doctoral degree in virology from Harvard. Largely because of this experience, Francis was among the first to suggest that the puzzling outbreak was caused by a retrovirus.

By this time, Francis was assistant director of the CDC hepatitis lab in Phoenix, Arizona, a location which grew problematic as he became increasingly involved with the frenetic work of the AIDS Task Force located at CDC headquarters in Atlanta. In 1983, he and his young family moved to Atlanta, where Francis became coordinator of AIDS Laboratory Activities and a prime player in CDC efforts to isolate an infectious agent.

Of interest is his frank account of the race to isolate a virus which involved, among others, Robert Gallo at the National Institutes of Health, the Montagnier group at the Pasteur Institute, Jay Levy at the University of California at San Francisco, and himself. It was a race with high stakes in terms of scientific prestige and money. Triumphal announcement by the United States of the isolation of a virus in April 1984 led to a bitter controversy over credit from which science and personal reputation did not emerge unscathed.

In addition to these headline events, Francis provides a picture of the often frenzied and frustrating conditions under which the CDC AIDS team operated in the first years of the epidemic. Francis is not alone in his view that Reagan's downsizing of the federal government resulted in inadequate national leadership and funding of early AIDS efforts. In addition to the strain of conducting research with meager funds and staffing, he and his colleagues were under constant pressure from the media to "explain" the epidemic, an essential burden in CDC efforts to educate the American public about AIDS.

The situation sorely tried those at the frontline. Speaking in the oral history of a CDC AIDS group nicknamed the Sextet,[1] Francis said: "...we spent hours trying to economize....The frustration would take all your energy away, and you needed immense energy to deal with this epidemic."

Upon his retirement from the CDC in 1992, Francis was completing terms as CDC advisor on AIDS to the state of California and special consultant on

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[1] Members of the Sextet were Walter Dowdle, John Bennett, James Curran, Bruce Evatt, Frederick Murphy, and Francis.

AIDS to San Francisco Mayor Art Agnos. In 1992, he joined Genentech as director of a team developing an AIDS vaccine. After these interviews were completed, the vaccine program which was spun off as a new company, Genenvax, which Francis currently heads.

Fascinating history indeed, but why, the purist might ask, is Francis included in a series on San Francisco's early medical response to the AIDS epidemic? The answer: to suggest that from the earliest days, local efforts to confront the epidemic simultaneously influenced and were influenced by events elsewhere. The federal institution most critical to local biomedical responses to AIDS was the Centers for Disease Control, and Francis was key to its early AIDS efforts.

The oral history of one individual cannot of course fully delineate the complex interactions between the CDC and AIDS scientists and health professionals at early centers of the epidemic. But because Francis was a central figure at an institution central to the science, epidemiology, information, and politics of the early epidemic, his story provides national context for the local efforts recounted in other oral histories in this series.

The Oral History Process

Three interviews were recorded with Dr. Francis between September 1993 and February 1994 in his office at Genentech. In shirt sleeves and slacks and looking younger than his fifty-some years, he provided glimpses in the interviews of the passion and purpose for which he is known. He borders on the charismatic, a fact which nettles colleagues who have also made significant contributions but who draw less public acclaim. He acknowledged off tape that the fame he acquired from his leading role (played by Matthew Modine) in the film of And the Band Played On was "embarrassing", but recognized its political expediency in his effort to win support for AIDS vaccine research.

Francis edited lightly, with no substantive changes. The oral history stands as an intriguing but incomplete record of the achievements of one individual and the institution he represented in the early years of the epidemic. In many senses, this volume is just a beginning but, one hopes, a tantalizing one which will inspire deeper and wider exploration of the CDC's contributions to the AIDS effort.

The Regional Oral History Office was established in 1954 to augment through tape-recorded memoirs the Library's materials on the history of California and the West. Copies of all interviews are available for research use in The Bancroft Library and in the UCLA Department of Special Collections. The office is under the direction of Willa K. Baum, and is an administrative division of The Bancroft Library of the University of California, Berkeley.

Sally Smith Hughes, Ph.D.
Research Historian

Regional Oral History Office
April 1997

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 Donald Pinkston Francis

Date of birth 24 Oct 42 Birthplace Los Angeles

Father's full name Cyril Herbrand Chalmers-Francis

Occupation Physician Birthplace England

Mother's full name Beth Tollan Pinkston

Occupation Physician Birthplace Manila, PI

Your spouse Karen Marie Starko

Occupation Physician Birthplace Regensburg, Germany

Your children Wm. Oliver Starko Francis
Stephen Starko Francis

Where did you grow up? Marin County, CA

Present community Hillsborough, CA

Education College of Marin → Univ Calif, Berkeley →
Northwestern Medical School → Harvard Sch. Pub H

Occupation(s) Physician

Areas of expertise Infectious disease epidemiology,
pediatric infectious disease, AIDS
vaccinology

Other interests or activities Carpentry, skiing,
hiking and social evolution

Organizations in which you are active

I FAMILY BACKGROUND, EDUCATION, AND EARLY CAREER

[Interview 1: September 30, 1993] ##[1]

Early Education

Hughes: Please give a brief summary of your life up until the time of the AIDS epidemic.

Francis: I'm a native Californian, actually a third-generation California physician, with my grandfather having come from England and practiced in L.A. My mother is also a physician. There was a whole California tradition of physicians.

I was born in Los Angeles on October 24, 1942 and raised in Marin County, across the bay from San Francisco, and then went to undergraduate school at the University of California at Berkeley [1961-1964]. I then moved off to Chicago to do medical school at Northwestern University School of Medicine [1964-1968]. I came back for my pediatric training [internship and residency] at L.A. County [University of Southern California] Medical Center [1969-1970].

It was the Vietnam War era, and I was staunchly and overtly committed to being against the war and against supporting the military. I was planning on moving to Canada, because I had applied for conscientious objector status, but very few people were getting it. I thought the odds were that I would not get it and that I would be 1A [the top draft category], and then I'd have to jump ship and be in an illegal situation. So I decided that it would be better if I went to Canada.

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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.

Employment by the Centers for Disease Control

Francis: I went to the chairman of the Department of Pediatrics in Los Angeles, Paul Wehrle, and asked him where he would get training in Canada. He said, "Well, why don't you apply for the CDC [Centers for Disease Control] Epidemic Intelligence Service?" I ultimately did, but because I'd been on a pediatric fellowship in India right out of medical school [1968], I was six months off. Usually it's July to July in medical training; I was going January to January.

State Epidemiologist, U.S. Agency for International Development, River's State, Nigeria, January-June 1971

Francis: So I had six months extra, and CDC then sent me to Nigeria after the Biafran War when things were so terrible in Nigeria. That's when cholera hit West Africa, so I spent my first six months for CDC fighting cholera in West Africa.

Epidemic Intelligence Service Officer, Oregon State Health Division, July 1971-December 1972

Francis: Then I came back and did my initial assignment in CDC, which was going to be for two years. They said, "Where do you want to be assigned?" Because CDC has a variety of assignments, either in Atlanta or out in the states. I said, "I want to be as close to the West Coast as I can," so I took Oregon, for no other reason than it was close to home. [laughs] It was actually supposed to be two years of training in epidemiology there.

Hughes: At the university?

Francis: No, it was at the state health department.

Smallpox in Yugoslavia, 1972

Francis: But it was interrupted; there was a smallpox epidemic in Yugoslavia in '72, I guess it was, and I got one of these urgent calls to hit the airplane straight away, and went off to

Yugoslavia. I spent, I guess, a few weeks fighting the epidemic there and stopping smallpox. I said, "Gee, that's really an exciting thing to do."

Hughes: Why were you chosen?

Francis: Probably because I had international experience, in India and Nigeria, and I had at least seen cases of smallpox, and I had worked in foreign areas. It was a team of about ten of us, I think, and we ultimately immunized the whole country, and I worked right down in the epidemic.

I met a guy named Bill Foege. He was this tall, thin, head of smallpox eradication for CDC. I met him actually on the opposite side of a volleyball court, which is the wrong way to meet a six-foot-seven individual. [laughter] But I told him, "If you ever do anything in smallpox, I'd be interested."

Hughes: Was there talk of eradication at this point?

Francis: No, the worldwide program hadn't been started yet.[1] Bill Foege and others had done some initial eradication program in West Africa, and I was really kind of an offshoot of that when I was in Nigeria. So I knew very well what they were doing. He really developed the concept of search and containment. Instead of trying to vaccinate everybody, the issue was to find cases and then do very compulsive, 100 percent vaccination around the cases. Then you could stop the disease instead of trying to vaccinate the whole world, which never worked, because you miss so many people.

Smallpox Eradication in Sudan, India, and Bangladesh, January 1973-June 1975

Francis: As I say, I said, "If you ever really want to do a big smallpox program, I'd be interested." So even before I finished my two years of training, I was called by the smallpox eradication program and was sent off for two and a half years to WHO [World Health Organization], initially in Sudan, then in India, and then Bangladesh.

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[1] See: Frank Fenner, Donald A. Henderson, Isao Arita, et al. Smallpox and Its Eradication. History of International Public Health, no. 6. Geneva: World Health Organization, 1988.

Research Fellow in Pediatrics, Harvard Medical School, and Doctoral Student, Department of Microbiology, Harvard School of Public Health, July 1975-November 1979

Francis: At the conclusion of my smallpox work--this was 1975--I felt very isolated from any modern medicine, and asked CDC to send me for some training. I talked them into two years of training for my infectious disease fellowship at Harvard. I was going to do a master's in public health at the same time, but then I decided that was really dull. I wanted to do some laboratory work. I had some very good advice from a guy named Roger Feldman at CDC to get a strong laboratory background.

Hughes: Which you hadn't had before?

Francis: Which I hadn't had. So luckily, the former head of epidemiology at CDC, called the father of epidemiology in the United States, a fellow named Alex Langmuir, was at Harvard at that time. When I came back from India, he set me up to have lunch with the School of Public Health microbiology faculty and see what projects they were doing--in case I was interested in them. We sat around with bag lunches, and everyone mentioned what they were doing. There were all these esoteric, mostly immunology studies, and then there was this one guy named Max [Myron] Essex who was working with cats and feline leukemia. I had become increasingly interested in the late manifestations of viral infections, these things that take years and years to develop.

Hughes: Why?

Francis: Because I think we all have this bias in virology that it's a two-week incubation period and you develop a disease. And I began learning more of chronic hepatitis, or possibly liver cancer, or herpes zoster after chicken pox, and these kinds of diseases that happen years and years after initial infection. I just was fascinated by the fact that an acute viral infection could produce a disease years and years later. Were some other diseases we see in adults really a function of pediatric infections years before?

Now realize, the only reason I went to Harvard was because I had met a girl in Portland, and she was an undergraduate, years younger than I was, at Harvard. So I was going back to see her, and I thought I would try to combine a personal advantage with my training. But we broke up when I was in Bangladesh, so by the time I got there, we weren't together anymore. So I found myself there for no particular personal reason whatsoever. [laughter]

Hughes: Well, it's a good place to be for no reason whatsoever.

Francis: I met my future wife [Karen M. Starko, M.D.] there, so it worked out very well.

Research with Max Essex

Francis: I started working with Max on feline leukemia, and I ultimately--another kind of chancy situation--talked CDC out of an extra year. So I was able actually to complete a doctorate in microbiology studying feline leukemia virus, which is a retrovirus. There were no retroviruses known in humans at that time.

Hughes: Was Essex's lab a retroviral lab at that stage?

Francis: Yes.

Hughes: Did that mean anything to you at that point?

Francis: No. It was just a classification of viruses. As a matter of fact, the infectious disease group usually stayed out of the whole retrovirus field, because it was dominated by scientists studying cancer viruses of mice that pass from mother to offspring, and it didn't really seem to make any difference to the field of virology. So it was always kind of a separate field.

Hughes: Had the myth been destroyed at that point, that retroviruses were animal pathogens, not human?

Francis: There was still the debate. They were pathogens, but they were thought to be vertically transmitted instead of horizontally transmitted. It was really some of Max's initial studies showing that these cats actually transmitted from cat to cat, not from dam to kitten, which indicated that retroviruses could be horizontally transmitted. And my work was really on working out the whole transmission and outcome, the natural history, of feline leukemia virus.

The CDC was fighting me regarding my third year of doctoral training. I had to finish all my laboratory work. I'd see my patients in the morning and then rush off in the afternoon to do my laboratory work. But I decided not to get a master's, so I really had nothing if I didn't get my doctorate. I was working towards the doctoral program, and completing my exams and such.

Then CDC said, "Well, we only promised to send you to Harvard for two years."

Ebola Virus in Sudan, 1976

Francis: Well, in the middle of my second year, I got this call from CDC saying, "We've got this really big problem in Sudan of this new virus that we don't know anything about. You speak some Arabic; you know Sudan well. Would you be willing to go?" I said, "My god, I'm right in the middle of my classes; I'm doing my research. How can I do this? But sure, if you need someone in Sudan, I'll go there." Then I said, "Well, what is it?"

They said, "Well, it's like Marburg virus." I knew what Marburg was. It was this terrible virus that came into Marburg, Germany, and killed all these people. It was one of the viruses that we kept in the high security area in the CDC. I said, "What! Why are you calling me?"

They said, "Well, you work with dangerous viruses." I said, "What, feline leukemia? Just because I work in a hood? We don't keep that as a class IV (highly pathogenic) agent." But they said, "Oh, you've got experience," and so I naively said, "Why not?" My father actually was living in London and came to visit that very night. He had never met [the person who] was to be my future wife. I had to say, "Well, it was good of you to come, but I've got to go to Sudan." So at least they got to spend some time together; I left straight away. [laughs]

CDC said it was going to be for two weeks. Well, this turned out to be Ebola virus in Sudan. It was, what, two months before we were ready to leave, and then we got thrown in quarantine for two weeks in Juba, Sudan. So it was a huge hole out of my academic year. But that loss actually served as the lever to make CDC support my third year at Harvard, ultimately allowing me to get my doctorate, so it all worked out fine. And I survived.

Hughes: Do you want to say something about Ebola?

Francis: That was an incredible thing to be involved in. First of all, we were quarantined out. The north of Sudan is primarily Arab and Muslim, and the south of Sudan is really black central Africa, with Christians and animists, local religions. They've been at war for years; they weren't when I was there. That was the only

period of time when they were not at war; they're back at war again and now it's horrible.

The north didn't seem to really care, so they just quarantined off the whole south, so the WHO team couldn't even get down there. There was a CDC team that went--a large team with helicopters and everything--into Zaire, on the other side of the border. But I was part of a WHO team which consisted essentially of two of us. [laughs]

Hughes: Who was the other?

Francis: David Simpson, from the London School of Tropical Medicine. He was very experienced; he had worked with Marburg a lot. Thank goodness, because he had all the isolation experience and knew how to survive in this environment.

Hughes: Would CDC have sent you there without proper preparation to deal with a lethal virus?

Francis: Yes, as long as there was a senior person there.

Hughes: So Simpson was essential; they wouldn't have sent two untrained people in there.

Francis: No, no. I learned you get military credit for being at CDC, because you actually end up doing some things that are far more dangerous than a doctor would ever do in a military setting, and this was certainly one of those instances.

We finally got a plane to take us down. Then it was about a twelve hours' drive directly west of Juba, which is way down by the CAR [Central African Republic]-Zaire border. We got down to Juba, and of course there were no vehicles ready. We had to get tires on the Land Rovers and get some trucks for all of our equipment. So it took us most of the day to do that, and we left about three or four o'clock in the afternoon, for a twelve-hour drive. There are no paved roads, and the rains were just ending. But unfortunately, it had rained just the day before, so we had this horrible muddy track to drive on until two or three o'clock in the morning.

The driver got exhausted about three-quarters of the way, so I drove the rest of the way. It was an incredible experience to go into this tiny town called Maridi out in the middle of nowhere, little government setting with a hospital and a few government offices. Eerie silence over the whole place. Luckily, there was a missionary family there that put us up, with at least a bed and some food. It was all quarantined out; no

food, no nothing was coming in. They had some fruit trees, so at least we got some food.

The first few days were spent seeing patients, with respirators on, in the hospital, and getting lists of patients. David was setting up the lab, doing the laboratory work, trying to get the right specimens. I did the epidemiology. I started visiting all the survivors and the families of the dead people, and tried to piece the epidemic together--to figure out how it transmitted. Because it was really scary. If there were airborne transmission, with that kind of virus it would have been deadly. I guess at that point, about a quarter of the nurses and one of the doctors had already died. By the time we finished, half the nurses in the hospital were dead.

Fitting it all together within a few days, I could really see how the disease transmitted. It was close contact with the blood of the dying or dead patients at funerals, or having sex with infected people. So at least it made us more comfortable going into these huts with these folks and wondering if you were going to die or not. The real danger was postmortem exams to get specimens. I did one on the ground in back of the hospital. It was really, really dangerous, and really stupid, when I think back on it. Because if we had stuck ourselves with one of those scalpels or any sharp instrument, it turned out we had a 90 percent chance of dying from a stick. Pretty high.

Hughes: You didn't know that at the time?

Francis: No. Well, you knew you didn't want to be stuck. Traditionally in new epidemics, it's the investigator or the lab investigator who are the second generation cases often. That's how you actually find out where the virus is.

Hughes: Where had it come from? Was that the end of the epidemic?

Francis: No, it came out again. We traced it down to a cotton factory in the south. Everyone else had a very close, explainable contact, except for a group of people working at this cotton factory in Nzara, which was about thirty or forty miles from Maridi, which was the hospital that everyone had come to. This group of cotton workers just worked in the cotton factory, no other thing in common. So we traced it down to the cotton factory, and there was a lot of controversy about that. No one believed it. It was stated as kind of a hypothetical source in the medical literature. The experts didn't believe it, until about four years later, when an outbreak started again in the same cotton factory.

We trapped bats and rats and mice and mosquitoes, and did a huge amount of work searching for the source of the virus, and never did find it. It will turn out some day to be some strange insect or plant virus or the like. We still haven't found out where it came from.

Hughes: Any clues about why it began to infect humans?

Francis: Yes. I wouldn't be surprised if it infected humans before the 1976 epidemic--silently, without being detected. It's actually much like AIDS: the ecology changed. They built a factory down there with lots of people and a horrible environment, full of dust and such. So if something was there, you could sure spread it around. And then the next thing was, they had these night clubs, kind of social gatherings, where the first sexual transmissions occurred in several people. Then the ultimate amplifier was the hospital.

The owner of this night club actually got sick, and he had enough money to be taken up to the regional hospital in Maridi. Once he got sick, he got the nurses infected, and the nurses got sick and would go to the hospital. In the end the hospital staff was all but eliminated. This was a training hospital, not the usual African hospital where you go in and die, often with very little intensive care. These were wonderful missionary-type nurses who were caring very closely for these patients. They all got infected, and their friends would take care of them, and they would get infected. It ultimately spread to Juba, and then ultimately the doctor went all the way to Khartoum.

Hughes: Well, what are some of the principles from this experience that are going to be useful in the AIDS epidemic?

Francis: Well, we already see the principles emerging, of tropical viruses that exist, that unique ecological changes often allow them to spread where they wouldn't have spread before. If these dangerous viruses emerge, we have to take a very aggressive approach.

We took a very aggressive approach to stop the Ebola epidemic. When we found it was spread by funerals, we prevented funerals, and we took care of the bodies. And that was just totally contrary to the traditions of the local folks, and they hated us for it. But that was a public health endeavor--something we had to do.

Hughes: You made that decision yourself?

Francis: No, the Sudanese authorities, together with us. They really are the power, and they made the decision. So no, you wouldn't do that as a foreigner. That is a fine line, whether you could get away with that or not. You certainly couldn't get away with it if you were a foreigner making that decision.

Hughes: And then you presumably returned to Harvard to finish up your dissertation?

Francis: Yes, I came back to Harvard. The CDC was saying, "Now, what do you want to do?" By that time, I was married to Karen Starko. She was interested in the Epidemic Intelligence Service program, the EIS, the same one that Paul Wehrle recommended that I join. That's how we met, and we started dating, and ultimately got married. She was interested in that program and was signed up for CDC, and I was looking for an assignment that would fit with my virologic background, especially dealing with viruses with late manifestations. But there were no retroviruses known in humans at that time.

Learning Laboratory Technology

Hughes: Do you want to say what you had learned about epidemiology and virology, and the technology therewith, that was going to be applicable to the AIDS epidemic?

Francis: Well, if you think about the whole chance occurrence of all this training--. At this time, I was still a CDC-type epidemiologist, which is kind of a quick-and-dirty epidemiologist as compared to the people I worked with at Harvard on my doctorate, who were really sophisticated cancer epidemiologists. So I got real strength in writing my thesis with these folks and manuscripts about using modern epidemiologic techniques--far greater than we used at the time at CDC.

At the same time, I developed, if nothing else, the vocabulary to understand modern virology, nucleic acid chemistry, all the things you needed to know for recombinant technology; at least I was able to speak it. I was still kind of a CDC virologist dealing with infectious diseases but not molecular biology, but I had to take all these courses and understand modern techniques and deal with them. Which at least set me up when AIDS came to be. If nothing else, I spoke the language of modern virology. One of the things we have today in science is this incredible specialization, each one of us with our own

vocabulary within that specialty. If you can't speak it, you're lost. It's really like speaking another language.

Hughes: And you had all that.

Francis: So I had it, at least.

Hughes: You had been exposed to the laboratory technology, as well?

Francis: Yes, that's what I mean by vocabulary, and the ability to use the tools of modern biology. But I never felt myself to be an accomplished laboratorian.

Hughes: Did you like lab work?

Francis: I loved the data; I hated the gruel. It's very boring, day-to-day repetitive stuff. It's an exciting experience getting the data; it's really fun. I didn't mind doing the procedures once or twice, but it was the repetition, over and over and over again, that's really dull. I luckily had a very good work-study student technician, Dawn Gazagian, who worked with me all the time. And I think in those two and a half years in the lab, we published something like seven or eight manuscripts. So it was really very productive.

Hughes: How much contact did you have with Max Essex?

Francis: Oh, every day.

Hughes: So he was really right there?

Francis: Oh, yes. He was wonderful.

Assistant Director for Medical Science, Hepatitis and Enteritis Division, CDC, Phoenix, Arizona, July 1978-September 1983

Francis: It worked out that Karen and I would go to Phoenix, Arizona, which was the location of the hepatitis part of CDC--hepatitis viruses, especially hepatitis B, and also what ultimately turned out to be hepatitis C, which fit into the category of agents that cause acute infection, produce jaundice in some people, and ultimately produce a lot of chronic liver disease, including cancer. So it fit very well with my field of interest of viruses with late manifestations.

Viruses and Cancer

Hughes: The connection with cancer was known at that point?

Francis: Yes. It was at least developing at that point.

Hughes: What was the status of the concept of the viral cause of cancer?

Francis: Still very much open. There had been these reports periodically in the literature of retroviruses causing cancer in humans, and they were always kind of pooh-poohed, never really panned out very well. So it was thought that all the work in retroviruses in animals was not very applicable to human cancer--it all came out of the National Cancer Institute. But it actually set up a remarkable knowledge of nucleic acid structure of human cells and viruses which, once AIDS was diagnosed, just [snaps fingers] sent it straight into a very rapid discovery phase following the model of other retroviruses.

One of my early articles out of Harvard in Journal of Infectious Disease talked about the possibility of these cancer-producing viruses being in humans, and reviewed the animal models.[1] I think what we had at that time was hepatitis B, and said, "We need to look for other bugs and diseases." It was an interesting article, in retrospect.

Hughes: Why were people so doctrinaire? If viruses cause cancer in animals, which had been known for a long time, why couldn't they cause cancer in human beings?

Francis: I agree. The one thing I learned working with veterinarians is they have lots of very interesting diseases, including viruses that cause arthritis, viruses that cause cancer, viruses that cause immunosuppression, viruses that cause a whole variety of other diseases that look very much like human diseases. But I think we in human medicine were doctrinaire and biased. That certainly came through in the AIDS epidemic where early on, people would just not believe that it was caused by a virus.

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[1] D. P. Francis, M. Essex. Leukemia and lymphoma: Infrequent manifestations of common viral infections? A review. Journal of Infectious Disease 1978, 138:916-923.

Robert Gallo

Hughes: Was Gallo's work well known at that point?

Francis: Yes. Actually, I knew Bob Gallo at that time. He was working with Max. He was primarily well known, unfortunately, for having reported a virus that caused cancer which was a laboratory contaminant and ultimately didn't pan out.

Hughes: It plays into the story, don't you think?

Francis: Yes, in a way. I wouldn't put him down for that alone--we can all contaminate in the laboratory. That's much more acceptable than trying to steal credit. That's a different issue.

Hughes: This is pop psychology on my part, but I would think from what I know about his personality, there would be a real drive to get past that one mistake.

Francis: Yes, there was. But I don't mind that drive, as long as it's an honest drive. It's when it's dishonest that it gets in the way.

Hepatitis B Vaccine Trials in the United States, 1979-1980

Hughes: Talk about the Phoenix laboratory and hepatitis.

Francis: All right. I had worked with hepatitis as a general epidemiologist in Oregon, but never knew too much about it.

I didn't even know much about Phoenix, Arizona, even though by that time my mother had moved from Marin County to Prescott, Arizona. One of the reasons I came back from WHO was because she was diagnosed as having cancer, so it all kind of fit. Good thing to be near her at that time.

So I started learning hepatitis. Now, there were two remarkable things about hepatitis B at that time. One, there was a large epidemic in gay men, because of, again, an ecological change, not a virus change; the virus had been around for ages. But the ecology of homosexual activity had changed with commercialization and urbanization of homosexual activity, so that gay men were having a lot more contact with a lot more gay men. The spread of sexually transmitted diseases was just astronomical--gonorrhea, syphilis, even gastrointestinal diseases, and hepatitis B.

And the second thing was that Merck Sharpe & Dohme was developing a vaccine for hepatitis B, and one of the reasons that CDC wanted me to come into this field was because of my experience with vaccines.

Hughes: Was this the recombinant vaccine?

Francis: No, this was the forerunner of the recombinant. It was a plasma-derived vaccine, which is actually the same--the essence of it is exactly the same. It's a surface protein of the virus. You can either purify the plasma to get this protein, which is actually still used in many parts of the world, or you can produce it by recombinant technology. This early vaccine was plasma-derived.

The question was to see if it worked. It looked like it produced pretty good antibody, but we didn't have any way to test it, except in a few chimpanzees; the virus didn't grow in culture. The pattern of HIV in some ways is different, but also in some ways very similar. There was an animal model in the chimpanzee to test the hepatitis vaccine. The hepatitis vaccine worked in chimps, and the decision was made to move ahead in humans--to see if it worked in them.

So I started this large vaccine study in gay men. The group at CDC in Phoenix was already studying the spread of hepatitis B in five cities--San Francisco, Los Angeles, Denver, St. Louis, and Chicago--and Wolf Szmuness and Cladd Stevens were doing similar studies in New York City. So we all started immunizing these gay men, half with a placebo and half with the vaccine, and then followed them over time to see if the vaccine would protect. And indeed, it was a highly effective and safe vaccine.

But in the meantime, in doing these studies, I got to know, at least peripherally, the whole homosexual scene. I say peripherally--it was really in great sexual detail, but I didn't understand homosexuality necessarily, except it was a lot of men having sex with a lot of men. As a straight man, I couldn't understand it totally, but they did it, and I accepted it. In California, we can be very tolerant. [laughs]

I guess we should bring politics in here about this time, because with the completion of those trials, we started seeing that the efficacy of the vaccine was really quite phenomenal.[1]

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[1] D. P. Francis, S. C. Hadler, et al. The prevention of hepatitis B with vaccine. Report of the Center's for Disease Control multi-center efficacy trial among homosexual men. Annals of Internal Medicine 1982, 97:362-366.

We had done major epidemiologic studies across the country looking at how much hepatitis really was type B that would be prevented by the vaccine, and what it cost. We came out with an estimate of about $1 million a day for the United States, and now we had a vaccine that was 95-plus percent effective in preventing it. We kind of used the same smallpox model: why don't we just go out and get rid of this disease? That was our plan.

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Francis: We had the tools, but as it turned out, we weren't going to be able to apply those tools because of political short-sightedness.

Hepatitis B Vaccine Trials in China, 1982-1985

Francis: I started working in China, where there really was a huge need. Hepatitis B virus infected 60, 70, 80 percent of the Chinese, and cancer of the liver was one of the primary causes of death in the middle of life. So they were very interested in studying hepatitis B vaccine. I started working with Dr. Xu Zhi-Yi in Shanghai, and Liu Chung Bo in Beijing, studying the efficacy of hepatitis B vaccine to prevent the last big chunk of transmission that remained in the developing world, which was mother to infant transmission. We did a major study there showing that we could use vaccine alone, give it in the first day of life, and prevent infection of the babies to about 90 percent.[1] And that really took care of hepatitis B; we could eliminate it.

At that point, all the data were available to begin to eliminate hepatitis B in the world. That process is, unfortunately, just starting now. It takes years and years and years to get going, but I think it's something that's slowly coming in the future.

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[1] Z. Y. Xu, C. B. Liu, D. P. Francis, et al. Prevention of perinatal acquisition of hepatitis B virus carriage using vaccine: Preliminary report of a randomized, double-blind placebo-controlled and comparative trial. Pediatrics 1985, 76:713-718.

II THE AIDS EPIDEMIC

First Reports

Francis: Then I got this call from Jim Curran at CDC in Atlanta about these funny cases of Pneumocystis in gay men.

Hughes: When?

Francis: May, June of '81.

Hughes: Had you seen the MMWR report?

Francis: June 5, I think was the date of the article.[1] Some days before that, or a week before that, Jim called. Jim and I had worked on the hepatitis B vaccine study. His group from the sexually transmitted disease division of CDC actually paid--we stole their money to do the study of hepatitis B vaccine. They had extra money, so we worked together closely. He was kind of the organizer and made sure it was all proper. I was more the doer and the protocol designer. It was a good collaboration.

Hughes: What did you think right away?

Francis: Well, I immediately called Max, [laughs] as you might imagine, saying, "You wouldn't believe what's happening; we've got this immunosuppressive disease associated with cancer in gay men." So Max and I started conversing--I think my first notes are actually in June of '81. He was saying that there was some work with Kaposi's sarcoma, looking at cytomegalovirus as a possible cause,

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[1] Pneumocystis pneumonia--Los Angeles. Morbidity and Mortality Weekly Report 1981, 30:250-252 (June 5, 1981).

and he sent me a couple of articles on that. We started talking, and the data started coming in.

Jim said, "With your background in feline leukemia and your experience with gay men, it seems to me that you really need to help us on this." I said, "Sure," not realizing what it would do to the rest of my life.

The CDC Task Force on AIDS

Francis: A task force was set up. This was a time when CDC had no resources at all. Nobody wanted to spare anybody from any of their projects, because they were already overwhelmed. So nobody could get any staff to work up this new outbreak. New outbreaks are usually CDC's bread and butter--people will line up to get into new outbreaks and find new exciting things. This one was exactly the opposite. No one, no supervisor at least, wanted to give their folks up--for good reason. Because at that point, the Reagan administration was asking us, "Would you be happy with a 10 percent cut or a 20 percent cut?" So it was just horrible. Some of our key junior staff were being laid off and fired, because there were no resources.

Hughes: Tell me about the task force: Whose idea it was, who was on it, and what you thought you were doing.

Francis: I think it was really Paul Wiesner's idea. He was the head of the Division of Sexually Transmitted Diseases. He came from King Holmes' group in Seattle to join CDC as the head of the sexually transmitted disease division, and he saw this epidemic was a problem. So he said, "Well, we've got to set up a task force," and he really volunteered Jim Curran and Harold Jaffe and Bill Darrow, and I think Mary Guinan was in his group at the time.

Hughes: Is this standard CDC procedure?

Francis: It is. When there's a new epidemic, you grab people who one, are available, and two, have background to fit the epidemic, call some senior folks to head it, and then call a bunch of junior folks to work on it. Absolutely typical. But it usually lasts for a couple of weeks or a couple of months. And that's at a time when you had the resources to be able to afford the interruption of one's ongoing work.

Here, we had no resources at all, and the problem lasted for years and years and years. Just to get a secretary, to get money

to buy an airplane ticket, to talk someone in the laboratory into processing a specimen, required pulling teeth--for every single step. And it didn't last for two weeks; it lasted for years and years. It was a horrible bind to be in.

But this task force was set up. Initially, we all had our other jobs, and yet we'd all meet--I would usually meet by telephone from Phoenix--and young EIS officers were sent out to investigate these cases. Then we set up some surveillance systems in the big cities to start reporting the cases. It's really the typical epidemic response.

Defining the Epidemic

Hughes: Talk in more detail about that, particularly in regard to San Francisco. What exactly did go on between the CDC and the local people?

Francis: Well, the first thing was to count cases. If you're going to start defining an epidemic situation, the first thing to do is to find out what you're going to call the epidemic, what case is a case and what case is not a case. It was relatively easy for this disease. There were severe opportunistic infections that had not been seen before except in immunosuppressed people, and so the case definition was set up [1982]. The case definition was a severe opportunistic infection in someone who did not have any underlying disease or chemotherapy.

Hughes: The task force set up that definition?

Francis: Yes. It's absolutely key in epidemic control to make a case definition to determine who fits in and who fits out. The other disease fitting the case definition was Kaposi's sarcoma. Previously that didn't occur in young people; by and large it was [found in] older, Mediterranean or Jewish males. For the original case definition of AIDS, as long as a person was under the age of sixty or sixty-five, I've forgotten which, and had Kaposi's sarcoma, we called him a case.

And then, we investigated the cases to find out in the broadest sense how they got their disease. Initially, that's often a kind of quick-and-dirty investigation. It was simple at first. Basically the forms asked, was the case straight or gay? And obviously, most people were gay. But soon there were some straight people who started coming through. Investigation of them led to the fact that they were intravenous drug users.

Hughes: But nothing much was made of that for a long time.

Francis: No.

Hughes: Why?

Francis: The unknown aspects of it. It was investigation, trying to figure out what it was, and you needed people to collect data, you needed information to be able to make your hypothesis of what kind of a disease it was. So the first year was spent actually doing an investigation of gay cases. Harold Jaffe designed and implemented a case-control study. I think the vast majority of all living AIDS cases in the United States were actually contacted by one of these young epidemiologists and interviewed, with a huge form; I remember it well. Your pets, and your sex, and your drugs that you took, a huge thing, trying to throw a very broad net to investigate risk factors for individuals who had the disease. Then in each one of the cities in which a case lived, controls were taken in the same community, and the same questions were asked of the controls, trying to see what the cases did that the controls didn't. It rapidly fell out that it was sexual activity.

Now, a similar study in New York showed that it was sexual activity, yes, but the use of amyl and butyl nitrite was also associated. That was "poppers"--a drug that causes vasodilatation, used for cardiac disease, that also was supposed to be wonderful for sexual orgasm. Poppers were very popular, and were sold over the counter as a deodorant for gyms or locker rooms--I don't know how. [laughing] I don't know if they were ever used for a deodorant, but that was the marketing ploy. People would just use them as a sexual stimulant.

Harold Jaffe rapidly said that the New York conclusion was wrong, that the primary issue here was sex, and people who have lots of sex look for sexual stimulants and use the drug. The risk was sex and the drug use that carried along with it.

Hughes: Why did he say that?

Francis: Well, there are very elaborate statistical techniques that are used to try to tease out primary versus confounding risk factors associated with any disease. Modern computers have allowed us to do that, where you can just run the data over and over and over again, pulling out different parameters. If someone is positive or negative for this question, you can actually pull him out and analyze that group separately, as if they did or did not exist. From this multivariant analysis, Harold concluded--and I think

logically--that poppers were a secondary factor instead of a primary one.

Resource Crisis

Francis: Well, unfortunately, the Reagan administration didn't want to hear any of this. They wanted an easy out for this epidemic, and continued to think that poppers were it, at least in terms of action. They didn't withdraw poppers, mind you. They did nothing. They didn't want to do anything. They didn't want to support any part of the investigation or disease control. I'm sure you're familiar with the memos that I've written blasting from Phoenix and Atlanta that we've got to have resources; we have to do this right; we can't let an epidemic as severe as this just burn. Because what was really coming through, and indeed was true from the first MMWR, was that it looked like once you got this disease, you died.

That wasn't typical of most diseases that we work with. Most people, even with bad infectious diseases, survive. You have to go to viruses like Ebola and rabies and others to get this kind of horribly serious situation. It was a terrible sandwich for a public health person to be in.

I wrote a remarkable memo in April '83, which Randy Shilts has in his book,[1] saying that we're sandwiched between a huge problem and inadequate resources. Secretary of Health and Human Services Margaret Heckler the same day was saying, "I've just checked with all my public health staff, and we're doing everything we can for this disease. No rock is being left unturned," and that kind of garbage.

So the administration was just horrible with this disease, leaving CDC, which was the premier investigatory institution for the world, not to mention the United States, really shackled.

Hughes: That particular memo that you wrote went to Walter Dowdle, chief of the CDC Center for Infectious Diseases. How did he respond?

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[1] Randy Shilts, And the Band Played On: Politics, People, and the AIDS Epidemic. New York: Penguin Books, 1988, p.273.

See also: James Kinsella, Covering the Plague: AIDS and the American Media. New Brunswick, NJ: Rutgers University Press, 1989, pp.179-181.

Francis: Well, Walt Dowdle then reported to Bill Foege, who was by then director of CDC--from smallpox to director of CDC--and they sent up budget requests to deal with this epidemic to the Assistant Secretary of Health, who I think was Ed Brandt at the time, and at that point the requests die.

It's interesting, you don't have to have a paper trail: If you're sitting in a director's office at CDC, and you're being told day after day to cut your staff, cut your budget, it doesn't take a rocket scientist to say, "Well, gee, when we apply for more staff, they're going to say no."

So this aura starts setting in of, "We're never going to get these resources from the administration to do anything." You sit there and argue with them about, "We need more vaccine for measles for children," and they say, "Why, we don't have any measles." Well, then a decade later we get this huge measles epidemic in the United States, and no one looks back at these jerks in the past who said, "Well, we had to save money," in order to buy more armaments, so that we couldn't immunize kids. You'll never hear, it will never come up in public, that someone back there was the villain by deciding that CDC's budget was too high; they were going to cut it back.

So I think the reality is the requests for funds were passed up to department level probably already cut down to what they would realistically expect, and then they disappeared into the never-never land of HHS [Health and Human Services].

Hughes: You never got an answer?

Francis: Oh, you got an answer.

Hughes: What was the gist?

Francis: "We'll never get these folks [the Reagan administration] to do anything." Everyone knew it.

Unfortunately, I think maybe, if you look back on it, one of our [CDC's] mistakes was being "team players." The team we were on was the team of the United States people; we were not on any team of government, in terms of a specific elected group. And yet, the way it's set up in democracies is that we [CDC] were not independent from the elected government or politics. And at this point, CDC becomes a very political organization. The director of CDC is now a presidential appointee, essentially a political appointee. That's not good. You need public health to be independent, and you need CDC to have an insulation from politics.

Now we've got the Clinton administration, and they're going to be very good policy setters for public health. And so there's no problem, and so things won't change. But someday, we're going to have another Ronald Reagan in there, and they're going to get control of an organization like CDC. I tell you, the damage done by Reagan to CDC will be felt as American citizens and world citizens for the next decade. Turning it around is going to take a huge amount of time. There are people like myself and others who were trained in the activist mode at CDC, and me, and all the rest are going to leave. As soon as they're retirement-eligible, they'll bail. Like me.

[tape interruption]

Here you are at CDC, earning half the money that you could elsewhere, fighting a bureaucracy that's often very frustrating. Why do you stay? You stay because it's fun and exciting, new stuff, stopping disease, stomping out viruses and bacteria and parasites. It's accomplishment that makes it fun. When you take that accomplishment away, then you're going to really select for people who are status-quo seekers, and status quo is totally contrary to the philosophy of public health.

Well, that's essentially what the Reagan administration was saying, "Let's figure out all the things we can't do instead of the things that we can do." Public health is always very cheap and does things with incredibly limited resources. The example that I used from that period of time, to put this in perspective, is that the budget of Mass[achusetts] General Hospital was the same as the budget of CDC, which was the same as the budget of WHO. So you can see where we put the priorities in terms of disease. We put it in therapy. The closer we get to large-scale prevention, the less resources we put in.

Risk Groups

Hughes: Let's get back to the framing of the disease, which initially as you well know was framed as a gay disease. Did you buy into that initial definition?

Francis: CDC, for good reason, never used the term GRID, which is gay-related immune deficiency, because very rapidly, the intravenous drug users surfaced. As infectious disease epidemiologists, never would we ever think of a disease--an infectious disease, at least--being exclusively associated with one group. It just doesn't do that. Now, you can have a unique infection of someone

who received dialysis, which would be only associated with kidney dialysis patients. It just wouldn't transmit in other ways. But not many other diseases would fit in that paradigm. Obviously, because of our bias, we immediately thought of infectious agents as the cause here, because we'd been working with gay men for years, and they just were kind of the flagship of new infections coming through.

Hughes: By "we," you mean you or the entire AIDS task force?

Francis: I think close to the entire task force. There were people who always said, "Well, maybe it isn't infectious, Don." But ultimately, I had to make decisions. We had limited resources, and we were going to search for the cause. We couldn't pursue every possible cause--infectious or noninfectious. Nature was telling us something. From the epidemiologic data, we had gay men with sex; we had intravenous drug users; we soon had sexual partners of intravenous drug users, and then we had the hemophiliacs. Nature was telling us it was infectious. How else could you explain the disease in these disparate groups?

Now, the hemophiliacs were unique in that they received plasma that was filtered to sterilize it--well, those filters will filter out anything from bacteria up in size, which was very useful, because now I didn't have to worry about bacteria or parasites as the possible cause of AIDS. I only had to worry about viruses. So this framing that occurs was very useful from the laboratory side, but it was very clear epidemiologically that those folks who were talking about poppers, or those folks who were talking about immune overload and all this garbage--and those folks were almost everybody outside of CDC, it seems--were just not looking at the data.

Problems in Communicating Data

Francis: Looking back at our failures at CDC, some of which were resource- or at least people-related, it's clear that we didn't market the data well enough. Everyone now looking in retrospect says, "God, wasn't this obvious that a virus was the cause of AIDS?" Well, I think it was obvious to us who were very familiar day in and day out with the data.

When we pulled groups into the CDC for updating, with the worst example being the blood bank folks, you'd bring them in and try to educate them in a day, and it would probably take a week's worth of education to bring them up to speed. We didn't

recognize that, because we were so close to the data. We'd sit and give these very cold, dispassionate slide presentations of what the data was, without really making any editorial comments, like, "Obviously, this is infectious. Gay men are having anal intercourse and putting semen up their rectums all across the country; the disease only exists right now in San Francisco and New York and Los Angeles; don't give me this immune overload stuff." It was nonsense. And don't give me poppers, because gay sex and poppers were all over the country.

And then came the hemophiliacs, who do reside all over the country, and they weren't only in New York, San Francisco, and in Los Angeles. They were everywhere--just like their Factor VIII material. So the epidemiology told us all of the story. It's just that some people refused to accept it.

Hughes: Is one of the problem related to funding, in that presumably if the results of the CDC case-control study of AIDS [in San Francisco, New York, and Los Angeles][1] had been released sooner, people would have more quickly accepted a viral etiology? Because of lack of funds, it took something like two years to tabulate the results, did it not?

Francis: A year. We were releasing data constantly--one of the things that just plagued us at the time were conferences. There were constant requests. We were so short-handed that we hated it when stories would break in the newspapers, where in public health, we usually use the media to educate the public. That's part of our job. But when that would happen with AIDS, there were what, a handful of us, and your telephone would ring off the hook for three or four days, and you got nothing done. That meant that everything else stopped. There was no one to take up the slack.

So we made this very bad precedent of saying, "Okay, the media office has to handle this stuff," which meant that the response then became watered down to a relatively uninformative base which was totally contrary to CDC tradition. CDC generally sends the New York Times [reporter] to the EIS officer doing the epidemic for information, and that's a great way to do it. I mean, sure young epidemiologists make mistakes, but one, they get educated--it's part of a training program--and two, the public gets the latest information.

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[1] H. W. Jaffe, K. Choi, et al. National case-control study of Kaposi's sarcoma and Pneumocystis carinii pneumonia in homosexual men. Annals of Internal Medicine 1993, 99:145-158.

Jim Curran and I and others--everyone wanted us to speak. "What is this AIDS?" Bring us to these big conferences. Ultimately, we all got so tired of doing these dog-and-pony shows. They were truly very important for marketing the message and would have really helped the public to understand the disease. But we could only do so much, if you wanted to do your other jobs. So it really was a resource issue.

See, we didn't get <u>any</u> money. CDC finally got $400,000 for AIDS in the summer of 1983. Exactly two years into the epidemic, we got <u>$400,000</u>. Now, just for laboratory equipment alone I could have spent all that. So all that money that we had been spending, those ten, twenty people working on AIDS at CDC, came out of other disease control programs at CDC. I came out of hepatitis; Jim Curran and his group came out of sexually transmitted diseases. It was just stealing from Peter to pay Paul, and then doing it inadequately, setting kind of a whole trend to do this half-assed.

Hughes: What you're saying is, the media went to secondary people who really didn't have the immediacy of the data?

Francis: Or didn't get any comments at all.

Hughes: The message wasn't getting out? Or it was getting out garbled?

Francis: Getting out weakly, without the strength of the CDC behind it.

Hughes: What did you want to get out?

Francis: I think in a new epidemic, you want to get every bit of new information out. "Now we have drug users with AIDS." "The gay men with AIDS are associated with high levels of sexual activity." Be very frank about it. Once blood safety became an issue, the media just [noise of fist against palm]. Now the whole issue of "them and us" stood out. Up to that time, they could do a "them" thing very easily: "It is all junkies and queers. What do we care?" Now, realize we at CDC had been working with junkies and queers for an awful long time and realized that you can have disastrous infectious disease situations, especially with gay men, if you ignore them.

Hughes: What do you mean by that?

Francis: That they can spread disease across the country extremely fast. Traditionally, a new disease came in to coastal cities and then would go into the more interior areas of the country.

Hughes: Yes, but there was no reason that the agent, which a lot of people believed was infectious, was going to be limited to the original four risk groups [gay men, drug-users, hemophiliacs, and Haitians]. The existence of risk groups implied that people in them are vulnerable, and people outside them aren't.

Francis: There are two sides to that. One, the disease was limited to clear risk groups. But two, the data indicated that the incubation period was long and therefore we may be missing some new cases spreading out. We knew early on that there was heterosexual transmission from intravenous drug users as women and babies came down with AIDS. But the issue was very different at that point. The political (not scientific) issue then became solidarity, and "them and us," and quarantine and isolation and all of the stuff that was starting to be bantered around.

Once CDC starts to do a weak job of both investigating and preventing the disease, then the state and local health departments do a weak job. They don't have the staff, to deal with the media, to deal with intervention programs and take action. And then appropriately, the population starts feeling left out: "We're not being protected." The vacuum is set; there's no defense for it, and the extremists move in.

Then the government is going to respond, as Reagan's staff constantly tried to do, by saying, "Yes, we are working on this disease. Don't worry, it's 'them' anyway." What should have been the message from the highest levels of government was: "You don't have to worry about getting this disease from buses, from breathing air, normal daily activities. This does not look like the plague, and don't shun these people and send every gay man or Haitian away." Because the Haitians were getting beaten on; gay men were getting beaten on. Politicians who were looking to really segregate these folks anyway were happy to use this epidemic as an excuse.

Even the Secretary of Health, [Margaret] Heckler, who was not known for her strength, came out and said, "These are limited transmission patterns, and you've got to have intimate contact"--which meant sexual contact; they couldn't say it--"to get AIDS." But that argument should have raised the issue, "Well, I'm a heterosexual having sex; am I at risk?" And yes, you could be at risk through sexual activity, and that's where the message kind of broke down. It kind of flipped from extremes. "It's just these people in risk groups [who are at risk for AIDS]; it's <u>nobody</u> else."

CDC always put data out, but did not necessarily market it terribly well where everybody could understand it. But what CDC

doesn't do is hide data. It was and continues to be a gay epidemic here. The San Francisco Health Department estimates that two-thirds of the newly infected people per year in San Francisco are gay men. And that doesn't mean that one-third are not important, but what's happened is everyone's trying to shift now, "Oh, it's all heterosexual transmission." Yes, there will be rivulets of infection going out into the heterosexual community, but heterosexual sex is not like homosexual sex. Most heterosexuals don't have these large numbers of partners. And even when you limit the number of partners in the gay community today, there's so damn much virus around there, when 50 percent of the population is infected, that you make two mistakes and you get infected.

Hughes: Had this marketing, the term you used, which was not good in the AIDS epidemic, been part of CDC efforts in the past?

Francis: Yes. We never called it that, but it was all part of our training; we would deal with the press all the time.

Hughes: So the epidemic didn't present a new problem in that regard?

Francis: No, but you get this almost omnipotent feeling in organizations like the CDC, that "I am the expert in this field, and I will study this. As soon as I figure out what it is, when I say this should be done, it shall be done." And that was really strange that we felt that way. It works relatively well with statutory requirements like immunizations for school. But when it comes to community norms, such as sexual norms, it is another matter.

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Francis: You (as a public health officer) bury bodies in Sudan; you do these things in real epidemics, and you have tremendous power to control the epidemic.

Hughes: What about smallpox? There you eradicated a disease.

Francis: Yes, we eradicated a disease. But in terms of time, [Edward] Jenner developed the smallpox vaccine over 150 years before we eradicated the disease. Hepatitis B vaccine was made, and twenty years later we still have barely started to eradicate the disease. Bacterial infection in meat, like Jack-in-the-Box, is an old issue that's gone on for ages, and we still haven't dealt with it, so we have these epidemics of food poisoning. We feel very omnipotent and powerful in the midst of a fast-moving epidemic when we decide to do something, and it's politically acceptable to do it. But for slower moving and long-term disease problems, we haven't figured out how to tune the politics so that

good things are demanded by the people and public health is utilized. So we [CDC] kind of waited for the opportunities to wake up the people and the politicians, and you can't wait for the opportunities with an epidemic like AIDS.

The Reagan Administration's Slow Response

Francis: Also, it's really easy to fail when someone tells you to fail.

Hughes: The government was telling you to fail?

Francis: When your boss says to fail. Now, some of us get angry at that, and some of us say, "Well, that's the system." In the movie,[1] there was this feeling that Jim Curran and I were very different. Well, we are very different in style, but I don't think Jim had any less anger, nor at this time has any less anger, than I do about the government's ineptness with this epidemic in the early days. It was terrible. We would sit there and scream and yell--at the wall, unfortunately.

Hughes: Did it hamstring you psychologically?

Francis: Oh, it sucks your energy from you. We had this group called the Sextet (that was Steve McDougal's term)--Walt Dowdle, John Bennett, Jim Curran, I, Bruce Evatt, and Fred Murphy. We'd sit for hours and hours and hours talking about what we were going to do and how we would negotiate this ten-dollar item or this twenty-dollar item, or what study should we do or which cancel in its place. I'd get through those sessions, and I would just be so drained that we had so much to do, and we were so busy already. Yet we spent hours trying to economize. Because we had to make these horrible decisions of what we couldn't do, it would just double-drain you. The frustration would take all of your energy away, and you needed immense energy to deal with this epidemic. I started to go to work at three or four o'clock in the morning so that I could be home with my kids at night.

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[1] "And the Band Played On"--A Home Box Office (HBO) film based on Randy Shilts's book by the same title, broadcast in September 1993. Matthew Modine played Donald Francis.

Research at the Phoenix Laboratory

Hughes: We've skipped some of the story. You were at Phoenix, and now you're talking about Atlanta. Why don't you talk about what you actually were doing in Phoenix?

Francis: In Phoenix, the CDC wanted me to direct the laboratory work for AIDS.

Hughes: Is it correct to call what you were doing, basic science?

Francis: This was pretty straightforward. The first thing you do with a new epidemic is stick material from patients in animals and get them sick, so you can try to get an agent out. And then you put it in culture and you try to culture the agent in an incubator.

Hughes: What was the Phoenix lab doing prior to the AIDS epidemic?

Francis: Phoenix was all hepatitis or viral gastroenteritis.

Hughes: So AIDS fit in neatly with what the lab was used to doing?

Francis: Yes, in some ways. We were searching out the cause of non-A, non-B hepatitis. Now, what was unique about Phoenix, it was kind of a square, one-story building of about a couple hundred feet each direction, and in the middle were chimpanzees and monkeys. So we had primates, the chimpanzees being incredibly valuable. We made a decision not to use them initially in research on HIV, which was too bad in a way. Later, we found that chimps were the only susceptible animal, although they never do get sick, but they do get infected. But I had marmosets. We were breeding marmosets. We were using them in hepatitis A, but they weren't very valuable at that time. So I first injected them.

Gary Noble, who was head of viral diseases at CDC in Atlanta, was officially in charge. We would make suggestions of what should be done, what animals should be inoculated, and then I said, "Well, I'll do monkeys."

Hughes: Why monkeys?

Francis: Guinea pigs and small animals didn't come down with any [AIDS-related] disease, so we moved up the chain to more expensive animals. It was very interesting when I asked to do that. I turned to our animal head, Jim Ebert, and said, "Look, I want to stick a couple of marmosets. How can we do that?" And god, their eyes opened, and they said, "Oh, that's really scary."

At that time in our lab, since we were the World Health Organization lab, we had this unknown hepatitis virus from Russian troops in Afghanistan, which turned out ultimately to be hepatitis E virus, that we injected into our animals. We also had non-A, non-B, which turned out to be hepatitis C, we were injecting into animals. All of which posed immense danger to the humans working with them. These guys were very comfortable with that. They'd done it for years--hepatitis B, hepatitis A, non-A, non-B, whatever. They were accustomed to doing it.

But when I came in and said, "I want to take this stuff out of AIDS patients and shove it into these animals," they very appropriately said, "Oh, my god. We've got to do something very different with this agent. This could really be dangerous." I said, "Look, guys, most people don't think it's infectious." And they turned to me, very wisely, and said, "Don, you think it's infectious. And if you think it's infectious, we think it's infectious, and we're going to be extremely careful."

So then I needed a $5,000 hepa-filtered enclosure to keep these monkey cages in. I think it cost $10,000. Well, CDC said, "We'll never get this money. How are we going to do this?" And, I needed to modify the animal room, because I needed an anteroom where you could come in, change clothes, go into the dirty area, wash off, take your clothes off, get the disposals [disposable clothing] off, throw them away, get back into your other clothes and go back out, so you don't take this bug everywhere.

"Well, we'll never get permission to do that," I was told. Luckily, we had a handyman on the premises there, and Bud and I just went and got two-by-fours and sheetrock, and he built this thing, without asking anybody. If we had to ask CDC for permission and for funds, it would have taken months. But we had to ask to get this $10,000--can you imagine? Here we were, this big laboratory, and all I wanted was $10,000. I had to write paper after paper to justify it. After months, we ordered it, and finally we injected the marmosets.

The Move to the Centers for Disease Control in Atlanta

Francis: Now, during all that time, Gary Noble and I are discussing what needs to be done, but I'm trying to stay relatively peripheral. There was a personal issue on this. Atlanta was considering closing the Phoenix laboratory and moving us to Atlanta.

Hughes: Why?

Francis: Reagan economics. "Why do you need another facility out there?" And it was a good question: Why the hell is hepatitis out in Phoenix? It was an old CDC building, and they started working with Indians and gastroenteritis. That got into hepatitis A, and once you started working on hepatitis A you work on hepatitis B, so that's why it was in Phoenix. They didn't have the facilities in Atlanta; they didn't have the space in Atlanta. But we were a hotshot lab and they appropriately wanted us there. But we had our families in Phoenix.

I had now been with CDC since '71, and this was now '81; I'd been ten years at CDC, and been all over the world, but had never been assigned to Atlanta. And I rather liked that. So there was an issue there. They kept saying, "Won't you run the AIDS lab?" I said, "I can't do it from Phoenix." They said, "Sure you can." But I knew what the issue was: They were going to pull me and my family back to Atlanta, and maybe ultimately the lab.

So I resisted that. I said, "Look, I'll do it from here and do what I can, but you guys have to run the Atlanta stuff." Well, ultimately it became ridiculous. I would go back to Atlanta, and Jack Obijeski--he now works at Genentech; he involved me in Genentech in the first place--was really the hotshot molecular biologist in the CDC. I would go to a meeting, and Jack would be there and a few others, and he'd say what needed to be done, and I'd go back to Phoenix and do my thing, presuming that Gary Noble would follow through. And then I would come back to Atlanta a month later, and check what had been done. Nothing would be done. They just couldn't do anything. They clearly needed someone there.

So they kept pressuring me and pressuring me, and I said, "Okay, okay, I'll do it." Then I started commuting. Again, I'd leave my family in Phoenix. So I'd spend one week in Atlanta and then one week in Phoenix. That was really horrible. I was exhausted; the family was exhausted; we had young kids at that point. My wife was head of infectious disease for the health department in Phoenix at that time. She had discovered the cause of aspirin in Reye's syndrome and was doing all that stuff, and here she was trying to be a mother of two young children. It was just god-awful.

So I finally gave up. I guess in September of '83, we moved to Atlanta. And soon after, the whole Phoenix lab was closed, and we would have had to move anyway. The chimps and the freezers and everything had to be put into airplanes.

The Laboratory

Hughes: What was your setup in Atlanta?

Francis: Horrible. In Phoenix, we never felt like we really had a state-of-the-art laboratory, but we had a relatively modern virology lab. When you were away from headquarters, you could spend some money and at the end of the year you'd get your hand slapped. "Oh, god, I'm sorry, I overspent my budget. I'll never do it again." And then you do it next year. In Atlanta, that just wasn't the case.

So I walked into this lab in Atlanta, and this is the Centers for Disease Control--a world-class center. It used to be one of the most outstanding laboratories in the world. And it was just a pile of junk. Old copper incubators, and no modern virology at all. Now, some labs in Atlanta were well equipped, but certainly not the one that I inherited. I got some of the leftovers of a couple of programs, and a few people--Ci Cabradilla, Paul Feorino, Jane Getchall--who were really interested and really good. So it was kind of an interesting combination--devoted people, too much to do, and too few tools with which to work.

Now, I was, by that time, the assistant director of the Division of Viral Diseases [September 1983-June 1985], which is the biggest division in CDC, and so I had access to a lot of people. But you just can't go out and steal somebody from influenza. You can't go down to the hot lab and steal somebody from the Ebola group. But what you do is you kind of interest the director of these labs in this new disease, and then they kind of help you with some of their technicians and equipment. It's just a god-awful way to deal with an epidemic like this, but that's the way I had to do it.

So we patched it together, and when we got the first $400,000, we finally bought some incubators and centrifuges and all the plumbing and stuff that you need. Safety issues were an incredible problem, because we weren't in the hot lab, and yet I knew we had something that was damn dangerous. I didn't necessarily want to be in a space suit lab, because that really inhibits you, but I wanted space where at least you didn't have tourists walking down the hallway. I didn't want anybody to die in my laboratory--including me.

Hughes: You had tourists in the hallway?

Francis: Yes. Not only had we tourists walking down the hallway, we had virus walking up the hallway in these disposal pans. Because our autoclave, instead of being in each lab, which would be usual for really a highly infectious material, was down at the end of the hall. So we had just simple problems with changing doorknobs and things that just never would be done; it would take weeks and weeks and weeks. Actually, not until after I left Atlanta did they put security doors in the hallway. But we all knew you could walk through the autoclave room and bypass the security doors anyway.

We were careful with HIV. CDC had had only one death, from Rocky Mountain spotted fever, several years before. It increases your caution. But other HIV labs have not been so lucky. Look at Gallo's labs: I think they infected two people up there.

Hughes: Were you scared?

Francis: Sure. But that was part of the job. I think probably some of the psychopathology that those of us in this field have is that we get a certain thrill from our jobs. You don't want to get infected, but you want to be on the edge. I'm a downhill skier, and that kind of extra little risk-taking must be part of our personalities. In public health we always talk about risk reduction. We are committed to that. But the work we do is risky. You don't want to be the one that gets infected, and you don't want anyone in your lab to be infected. But you know that on the other side of your gloves is something very dangerous.

Suspecting a Retrovirus

Hughes: Talk to me about the science. What actually were you doing?

Francis: Well, I had been sending specimens to Max, so that by the time I got to Atlanta, we really were talking about an agent growing in lymphocytes that could well be a retrovirus.

Hughes: Why were you talking about a retrovirus?

Francis: Well, it was interesting. Max had done this interesting study where he took our sera, and he put that serum on HTLV-I-infected cells. This one technician named Mary Frances McLane in Max's lab could get a positive test on these cells in a high proportion of AIDS cases. We published that, actually, in the same journal

that the French published the LAV article--Gallo's articles on HTLV-I, Max and the CDC's article.[1]

Hughes: So that was 1983?

Francis: That was May of '83.

So since it was a lymphocyte-related disease, and since the retroviruses clearly were known to infect lymphocytes, we accelerated our search. Unfortunately for us, all our animals were thriving. We went all the way up the phylogenetic scale to monkeys and then ultimately to chimpanzees, but all were doing fine. That really hurt us in terms of finding a cause. If you don't have an animal that gets sick--.

I used to always run into Joe McDade in CDC, who's the one who found the Legionnaire's bug. And he would always be so sympathetic. He said, "Don, our guinea pigs bellied-up in six weeks, so we had something to work with. If you have two equations and one unknown, you can figure out what the unknown is. But when you have two equations and two unknowns--." We didn't have any antibody; we didn't have any antigen; we couldn't do anything. In retrospect, we made mistakes. Given our lack of resources, we never had time to think about what we were doing, whereas the French sat down and did it right.

Anyway, Max and Bob Gallo and I were all doing the same thing. We were culturing lymphocytes, putting fetal cord lymphocytes in with the patient's lymphocytes, and doing reverse transcriptase assays on them to see if a retrovirus would come up.

Hughes: What made you think it was a retrovirus?

Francis: It wasn't anything else, [laughs] I guess was one reason. We had retrovirus experience, and it fit in terms of a model. And Max's preliminary results in serology. Probably Max's preliminary serologic results were the most exciting. Bob was isolating HTLV-I, but we absolutely knew it was not HTLV-I.

Hughes: Why?

Francis: Because early on we'd sent blood specimens to Bob Gallo's lab for HTLV-I testing, and only 6 percent of them tested positive. It

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[1] M. Essex, M. F. McLane, T. H. Lee, et al. Antibodies to human T-cell leukemia virus membrane antigen (HTLV-MA) in hemophiliacs. Science 1983, 221:1061-1064.

didn't fit. We all thought it a was variant retrovirus of some kind at that time.

Hughes: Well, Shilts says that very early on, in 1981, you made the correlation with feline leukemia virus.[1]

Francis: Yes, it was very early. Actually, Dave Morens, who was doing the lab coordination for Gary Noble early on, actually published in JAMA a few months back that I said to him it was a retrovirus ages and ages before.[2]

Hughes: What was the date?

Francis: He actually dates it exactly. I don't remember what it is, though.

At the first Public Health Service meeting on the cause of the epidemic [Workshop on KS and opportunistic infections, September 15, 1981]--it was a small group of us, mostly from NIH and CDC. Shockingly, most of the interest was generated by Gene Shearer from NCI who was talking about semen up the rectum causing immunosuppression in rats. We had a one-day meeting, and the whole morning was spent on antigen overload and poppers as a possible cause of the epidemic.

I went up to the library at noon and made copies of my feline leukemia work and my hepatitis B epidemiology work. When it finally was my turn in the afternoon, I pulled them out and said, "If you combine these two, you have the epidemic. Everything fits. The virus with the epidemiology and transmission of hepatitis B, and the natural history of feline leukemia. You have it."

Hughes: What was the reaction?

Francis: Absolutely fell like a lead balloon. Talk about a marketing mistake! I'm sure I did it in about as much time as I just described it to you. I should have allowed more time, given more background, described what feline leukemia was.

Hughes: Why wouldn't your suggestion be followed, when they were considering poppers and immune overload, et cetera?

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[1] Shilts, And the Band Played On, p.73.

[2] Morens, D. M. Mandatory testing for HIV. Journal of the American Medical Association, March 3, 1993, v.269, 9:1115-1116.

Francis: Don't ask me. Back in the lab, I kept being influenced by those who kept pleading, "Well, we better think broader." More fundamentally, I didn't spend the time when we were culturing the virus to realize that we were not talking about a transforming retrovirus, like HTLV-I which produces cancer. We were talking of one more like feline leukemia that killed cells.

But it didn't make any difference, retrovirus or not. I was an infectious disease doc, trained in cytopathic viral disease. Max and Bob Gallo were retrovirus-transforming-type docs. We spent months putting AIDS samples on cell cultures and looking for rapid cell death--classic virology. Then when we switched over in the extreme to culturing lymphocytes, looking not for rapid cell death but for cell transformation, we followed the Gallo transforming protocol. I still don't know why I was influenced to make such a radical change.

Hughes: Is that what the French did differently?

Francis: Yes. The French looked early for reverse transcriptase elevation, signifying a rapidly growing cytopathic virus. They put specimens from patients in culture and frequently did RTs [reverse transcriptase assays] early after initiating the culture. We did not do testing that frequently. It was expensive to do the assay and we didn't have the resources. So we spread them out. Usually on the first one, a few weeks after infection, we got this small blip of elevated reverse transcriptase. Unfortunately we ignored it, because we were waiting for elevations weeks later as the virus transformed the cells. As a result, we missed the indication that we were growing the virus. It was there in that early blip. We were, in this case, too patient.

Isolation of the AIDS Virus

[Interview 2: December 22, 1993] ##

Associations with the Pasteur Institute

Hughes: Dr. Francis, we were talking last time about the isolation of the virus. I want to start today with your memory of your first association with the people at the Pasteur Institute, and why that came about.

Francis: The initial contact actually originated from Pasteur. As I recall, it was Françoise Barré who called me from Paris about some specimens that we had reported in our May '83 article with Essex. We went to the freezer where we kept San Francisco City Clinic cohort specimens and pulled out samples from individuals who developed AIDS. We had the early specimens and the late, because we'd been following these men as part of longterm hepatitis B studies.[1] Françoise was interested in these, because obviously if they were trying to make an association of a virus with AIDS and developing a test for AIDS, one of the conditions of proving the cause would be that the infection occurred at an appropriate interval prior to the onset of the disease. So you'd really like specimens from people many years before they came down with disease. We fortuitously had these specimens.

So Françoise called me--it must have been in mid-'83--and asked for some specimens. I said sure. So I sent her four specimens blinded. There were a couple of drops of serum of each of these very valuable specimens from two people who developed AIDS. There were two early specimens and two late specimens.

Hughes: Where were you getting your specimens?

Francis: From our freezer. [laughter] We had ongoing hepatitis studies. But because of our move from Phoenix to Atlanta, the freezers were all disorganized. Since we had no resources to hire someone to help, I had to literally go in and spend a day in the freezer with my winter clothes, sorting the specimens and getting them organized so that we could find the right ones.

Hughes: You were working exclusively from the hepatitis B specimens?

Francis: Well, we had lots of AIDS specimens at that point, but the French also had access to similar ones. More interesting were the hepatitis specimens where we had people who had a blood [specimen] taken early on and later developed AIDS.

Hughes: Then what happened?

Francis: I think a couple of months went by, and Françoise called me and said, "I have the antibody test results. Do you have the code?" I said, "Sure," and she gave me the results, and I gave her the code. She got all of them right: the two early ones were

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[1] For more on these studies, see the oral history with Paul O'Malley in The AIDS Epidemic in San Francisco: The Response of Community Physicians, 1981-1984. Regional Oral History Office, Bancroft Library, University of California, Berkeley. Hereafter, AIDS Community Physicians series.

negative and the two late ones were positive. So my interest in their virus increased dramatically. Initially we set up collaboration where Françoise came over and brought us virus to inoculate into monkeys. At that time we did nothing else with the virus besides inoculate; that was the agreement.

Hughes: Why? Did they limit it just to inoculation?

Francis: No, there wasn't much virus available at that time. It just kind of evolved. We just never moved any further than that early on. I got the feeling that they wanted to do the initial work. They wanted to feel comfortable with their findings before sending out samples to others. It wasn't until February of '84 that we got sizeable quantities of really hot-growing virus. By that time, they had enough virus to give out. They were producing enough to use in an antibody test. I was sending them specimens regularly and they would test them, and had quite good results.

Cold Spring Harbor Meeting on HTLV, September 1983

Francis: In September of '83, we had the first Cold Spring Harbor meeting on HTLV [human T-cell lymphotropic virus]. The French reported the results of the first four San Francisco City Clinic cohort specimens at that time. Then, we continued to send them other specimens, and their results were continuing to look quite good--relatively low positivity in the AIDS patients, but that was not surprising, because the immune system in the AIDS patients was already compromised. So it was not too surprising that they would have a lower level of positivity in that group compared to patients with lymphadenopathy.

Hughes: Was that the meeting where Montagnier first presented LAV [lymphadenopathy associated virus] as the possible cause of AIDS?

Francis: Right, that's where Montagnier initially presented the LAV results in public where, I think, they had 30-40 percent positive on their blood test with AIDS patients, and 80-90 percent positive with lymphadenopathy patients. And they had electron micrograph pictures of the virus, showing that it looked like a lentivirus. They were making parallels between that and the lentivirus of horses that causes equine infectious anemia.

Hughes: This comparison was based on the electron micrographs?

Francis: They were also doing some serologic comparisons, but primarily the lead was from EMs. It was such an unusual-looking bug that it looked like the horse lentivirus.

Hughes: What was the reaction from Gallo and the rest?

Francis: Gallo was really obnoxious. The rest of us were saying, "Well, it's interesting; it's worth pursuing." It looked exciting and interesting but not overwhelming at that point, because of the lower rates of positivity in the AIDS patients.

Hughes: Were you buying Gallo's hypothesis at that point, that the agent was an HTLV [human T-cell lymphotropic virus] of some kind?

Francis: Max Essex at Harvard was helping us--doing work with HTLV as the target virus against which we were testing serum from AIDS patients. But we knew it was not HTLV-I itself because Gallo had already done tests collaboratively with Max and me, and only 6 percent of the specimens were positive. So the cause was not HTLV-I. Our hypothesis was that it was a variant retrovirus, different but with some cross-reactivity to HTLV-I. It turned out to be even more distant than that. We were clearly very close to target, but it was not HTLV-I itself. And I think everyone knew that. Bob was pushing the HTLV-I concept more than Max and I were. We knew it was something like HTLV-I; our assumption was it was something like that, but not that very one.

Laboratory Procedures for the AIDS Virus

Hughes: Well now, last time you talked about the parallels with feline leukemia virus, and the fact that your lab protocol was still governed by the paradigm that [the AIDS virus] was a transforming virus. Why did you stick with that idea?

Francis: Because we were stupid. [laughter] HTLV was the only growable human retrovirus at the time, so it's logical that if you were looking for one retrovirus, you would use a protocol that worked for another human retrovirus. But we didn't take the ten minutes that it really would take to think about it: that it was not a slowly evolving transforming agent, that it was a really rapidly multiplying cytopathic agent. Instead of transforming cells making them cancerous, it was more likely to be cytopathic, killing them. If it were [transforming], it would show itself after a few days of culture rather than a few weeks or months.

Hughes: Where were you getting the fact that it was cytopathic?

Francis: Because the pathology of the disease was that it wiped out T cells.

Hughes: All right, so that was clear. So you didn't have to go into the RT business to establish that fact.

Francis: No, RT was just a measurement for a retrovirus growing in culture, and that's what we were doing. We were doing RTs on a regular basis, carrying on for months and months and months. It's kind of an arduous job, so you want to spread out the assays. So we didn't do them close together in the first few weeks. As I mentioned, we had little blips early. We had a little increase in RTs at that time, and we ignored it and waited for this big RT transformation later. Now, if we had just fed those viruses more substrate, if we had given them more cells to grow in during that early RT blip, we would have found the virus a year before.

Hughes: But that was the mistake that everybody was making.

Francis: Yes, we all made it.

The Pasteur Group's Approach to the AIDS Virus

Hughes: It's very easy in retrospect to say it was a mistake--

Francis: It's very easy in retrospect. But the French used logic and said, "Well, let's look early on. Let's not wait such a long time for RT to appear."

Hughes: How much do you think the flexibility of the French has to do with not buying into Gallo's hypothesis?

Francis: No, they have told me that they kind of did their work as a "Me, too" experiment. They said, "Gallo and CDC and Essex are all growing it, are getting a retrovirus; we'll just do the same thing that they're doing, and grow it too, just for interest's sake." But then when they sat there and designed their experiment, they put a little more thought in it than we all did. We were following the same old Gallo protocol. They said, "Well, let's just really zero in on the early stage of culture." They didn't realize that we were waiting and waiting and waiting for these transforming agents.

So they had a flexibility, but they also didn't have the bias that we did. And we were just totally overwhelmed with all

sorts of other things at the same time--and that's typical, when you're in a rush like that. You just don't sit and discuss everything and really outline it, and then kind of relax the way you need to in order to search appropriately.

Hughes: Am I right that the French group was focusing on the virology, not trying to do a lot of other things, as you at CDC were?

Francis: Right. They were just doing retrovirology of the specimens, whereas we were doing all sorts of other stuff, and a lot of animal inoculations and looking at other viruses. We had a very broad approach. They did it narrowly--but properly.

Hughes: Who do you credit with the realization that this was a different, a new, virus?

Francis: I think that you have to give the French the credit.

Hughes: Who specifically?

Francis: I don't know, [Luc] probably all three of them. It was Barré, [Jean-Claude] Chermann, and Montagnier--and it was Barré and Chermann I think that really did the virology. As I understand it, Montagnier's lab didn't want to grow this virus, which was probably a decision of laboratory safety. This is not a friendly little virus to grow in any casual way in a laboratory. You have to be very careful or you'll die.

Hughes: And yet, the Pasteur has a long history of working with lethal viruses. Think of rabies, which started it all off.[1]

Francis: As a matter of fact, the lab at Pasteur is right over Louis Pasteur's tomb. Françoise Barré and Jean-Claude Chermann were in the same building, and the tomb is right down in the basement. So the discovery was not far away from his remains.

Hughes: What difference did the conceptual framework of these three groups make? You and Gallo were using the HTLV framework and the Pasteur Institute group wasn't.

Francis: Oh, it's interesting. Willy Rozenbaum told the Pasteur group that he had a patient with lymphadenopathy and asked them to look at the tissue for a virus. They did it because they knew what we were doing and they were just going to repeat our work. They luckily didn't call us and ask us exactly what we were doing;

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[1] The Pasteur Institute was founded in 1888 to develop Louis Pasteur's rabies vaccine and eventually other vaccines.

they sat down and thought for themselves. Françoise Barré-Sinoussi and Jean-Claude Chermann, I think, are the ones who put it together, saying, "Well, we should really look early at the cell cultures, because the virus might be cytopathic."

Chermann's Presentations in the U.S., February 1984

Hughes: In February of 1984, Chermann came to the CDC. He gave a presentation at that time?

Francis: Yes, two presentations. He gave a presentation at Park City, Utah [February 7, 1984],[1] showing their data at that time. He reported much higher rates of positive tests in AIDS patients than before. He then gave the same talk at CDC on February 15. It was extremely convincing, and at that point he brought us virus (LAV). As a matter of fact, when he came in the country, I had arranged for our quarantine people in New York to pick up the virus and ship it down to us. By the time he arrived in Atlanta, we already had electron micrographs of it, and we started duplicating a lot of the work that he had done to show that this virus really was different. It was a lentivirus; the structure was similar to other lentiviruses--a subgroup of retroviruses.

At that point Chermann went back to our electro-photomicrograph pictures from our early cultures. That was one of the best and worst days of my life. Those pictures were taken back when these low-level RT values were detected. We had taken some electron micrographs of the cells at that time. He goes back and points at these structures in our EMs, "There's the virus right there."

Hughes: The virus was very clear?

Francis: Oh, yes. [tape interruption]

We had a picture of the virus in those early cultures, right there in front of us, and we missed it. It was in the cultures when we had these low levels of reverse transcriptase.

Now mind you, if you don't know what you're looking for with an electron microscope, it's very difficult. We had the best electron microscopists in the world working on it. But once you

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[1] John Crewdson. The Great AIDS Quest. Chicago Tribune, November 19, 1989, p.10.

knew what the virus looked like--it's a rather strange-looking thing--it's easy to spot. Jean-Claude said, "Look at this." And he was absolutely right. So, we had grown it. But we just missed it.

After Jean-Claude came, everything went like crazy, because we knew what we were doing. By early 1984, Bob Gallo calls and he says he's got [an antibody] test, and we had a test, and so we all were sending tests around, and that's when the misery started.[1] [tape interruption]

Hughes: Did you go to the Park City meeting where Chermann gave a presentation that February?

Francis: No, I did not. Jim Curran did. I don't remember if other people from CDC went.

Hughes: What was the reaction at the CDC meeting? Did people buy the LAV hypothesis?

Francis: Oh, yes. I think everyone at CDC knew the search was over; the cause had been found.

Distributing CDC Virus Specimens

Hughes: Two weeks after the Park City meeting, Gallo called to say that he'd found the virus.[2] Do you remember that?

Francis: I think I was talking to Max, who said that Bob had several isolates. And then Bob called Jim Curran--I've forgotten whether I was out of town or not--and said that he had developed a test and wanted some specimens from us. Jim talked to me and I arranged to send a panel of serum up to him.

Hughes: But you didn't ask for any specimens from him?

Francis: No, not at that point. We didn't know what he had and how useful it was. It wasn't until after the results came back that it was interesting.

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[1]For better chronology, the preceding three paragraphs were moved from the transcript of Interview 1.

[2] Sandra Panem, The AIDS Bureaucracy. Cambridge, MA: Harvard University Press, 1988, p.40.

Hughes: You mean the results from what you'd sent?

Francis: Yes.

Hughes: Interesting in what sense?

Francis: I took the same panel of serum; sent it to Bob Gallo, sent it to the Institute Pasteur, and sent it to our lab at CDC--all blinded. I kept the code, and then had them all report back to me the results of the antibody tests. The results proved that the cause of AIDS had been identified. The specimen panel was set up with some very valuable specimens, including the San Francisco city clinic cohort seroconverters and specimens from the transfusion-associated cases. For these we had samples from all the donors to a case of AIDS, and samples from the case of AIDS. If the blood tests were correct, you should be able to pick out the suspect donor to the case. And indeed, in all these cases, the suspect donor tested positive.

Hughes: So every place that you sent the panel got the same--

Francis: Came out with the same results, almost identically. We had a few plus or minuses, and a few variations which you'd expect on a new test. But that sewed the whole thing up.

Meeting at the Pasteur Institute, Early April 1984

Francis: That's the point where I called Bob and Pasteur and arranged for a meeting at the Institute Pasteur in early April to discuss how we were going to deal with all this.

Hughes: That meeting was contentious, was it not?

Francis: It was bizarre. Contentious only that Bob was not very sharing, excluded me from the discussions of his results with Pasteur, so I never did get to see his results until the preprint came out.

Hughes: What excuse did he use for excluding you?

Francis: Didn't want me to see his information.

Hughes: You mean he said that point blank?

Francis: Yes. He said something like, "I want to have the meeting with Pasteur in private."

Hughes: So he obviously thought of you as a competitor rather than a collaborator.

Francis: He saw both of us as competitors.

As a matter of fact, it got even more bizarre. Because everything was so exciting, we went out and celebrated that night. Jean-Claude took us out to a wild French cabaret. At that point, I didn't know, but Bob and Jean-Claude went to the restroom and Bob turned to him and said, "We're really doing well. Pasteur and NCI [National Cancer Institute] can do this together; we don't need CDC." And then the next morning alone with me at breakfast, he told me that CDC and NCI could do this; we didn't need Pasteur. So he was playing everything to his benefit. But it didn't take Jean-Claude and me too long before we shared that information.

But the sad thing is that when you have a bizarre person like Bob, who has some talent no doubt, and tremendous influence on the field, you give him extra leeway. We gave him far too much. Given his strange personality, all these kinds of things become expected--and accepted. So: "Oh, that's Bob; we'll go on our way. He acts like a seven-year-old child, and, well, we'll just have to tolerate him."

That was silly for me, to be honest. Here I was with Gallo in the Public Health Service in the U.S. government trying to find the cause of AIDS, and this guy was acting like a total lunatic. I should have reported him to the higher authorities straight away. But you kind of work with people as collaborators and not in some hierarchical government structure. That's one place where I should have shifted gears and said, "Enough's enough." Anyway, as you know, the insanity over the discovery went on and on for years.

V. "Kaly" Kalyanaraman

Hughes: Tell me how Kalyanaraman [Kaly] fits into this story, because it doesn't seem to me he's given enough credit.

Francis: Oh, no, he was very key for us in CDC. He's a very talented retrovirologist who was working in a contract laboratory in Bethesda that contracted with NCI and Bob Gallo. We put out the word at the National Cancer Institute that we were looking for an experienced retrovirologist, because we really thought a retrovirus was the cause, and we needed someone to help. We

finally got money (the Reagan administration finally, after two years, gave us I think $400,000), so we had money to support a Ph.D. level researcher.

Hughes: This was 1983?

Francis: This was 1983. We were recruiting a scientist from NCI named Shushil Devare, a very good guy, who was also being recruited by Abbott Laboratories. He was from the lab that Ci Cabradilla at CDC worked with, and Ci knew him. So we had Shushil come down for an interview. He would have been terrific. But he decided to go to the private sector, to Abbott.

Shushil passed the word amongst his friends, happened to be Indian friends, that CDC was looking for somebody, and Kaly called. Now, as soon as Kaly started looking into this job at CDC, I knew there was a potential problem, because he was working under a Gallo contract. Kaly was the discoverer of HTLV-II together with Bob Gallo. Recognizing the sensitivity, I called Bob straight away--as soon as I heard that Kaly was interested. I said, "We didn't recruit him, but he found out through a friend." I wanted to inform Bob about this, as a gentlemanly act--I mean, when you start dealing with other people's lab workers, you have to do it rather gingerly, because it's obviously a very touchy thing.

But we didn't initiate the contact, and I just told Bob, "We didn't initiate it, but Kaly's interested, and I will look at him seriously. If he's interested, that's up to him, not either you or me." He said, "Well, I will obviously urge him to stay," and I said, "Of course." He said, "I think he's very good." And that was it. Kaly ultimately decided to come to CDC.

Hughes: Why?

Francis: I don't know. I think he saw this as an opportunity for him to get out of a big lab setting. He didn't have a full-time position with NCI; he was a contract worker at another laboratory. And here he could have a full-time position at a good salary that NCI apparently couldn't offer him. So we hired him.

When the offer was made, I called Bob Gallo and said, "We have made an offer to Kaly," and he just hit the roof. Screamed and yelled at me, and said, "Kaly will come with no reagents. You will never get anything published in retrovirology; I will see to that. I find this terribly offensive." And he just went on one of his rampages that he often does. He screams and yells and abuses everyone in sight, including me. I said, "Well, thank

you very much, but that's not going to interfere with us hiring him." So Kaly came, and he was very valuable.

Hughes: What did he do specifically?

Francis: He was one of our primary virologists. He was isolating viruses from American [AIDS] patients' material; he would grow the virus, characterizing the viral proteins. He's a virologist/biologist and a protein chemist. So he was critical in purifying the virus and seeing what it looked like inside, improving serologic tests, et cetera.

Hughes: Was he using the technology that had been developed in Gallo's lab? By [Mikulas] Popovic and others? Or was that something that he brought to them?

Francis: The technology of tissue culture and cell culture is very widespread, some of which he was doing at Gallo's lab.

Hughes: But there were some specific cell lines that were used.

Francis: Yes, and a lot of that was done at NCI, I think most of it outside Bob Gallo's lab. But the specific techniques used at CDC in growing the virus were primarily the French techniques. That's what we used.

Hughes: Which techniques was Kaly using when he was on contract to NCI?

Francis: I don't think Kaly was working on AIDS at NCI. I'm not sure, but I think he was working on HTLV.

Hughes: I see. What I'm trying to find out is whether he came with the technology, which he then inserted into the CDC protocol.

Francis: No, he came and he really adopted the French protocol. And he combined their information with his vast knowledge of working with these viruses and their proteins. No doubt some of his skills were acquired while he was working at NCI. That's fair enough; that's progress.

Mikulas Popovic's Pooling of AIDS Sera

Hughes: One other point: there has been criticism of Popovic's method of pooling serum.[1] What is your opinion, and how unusual is that technique in virology?

Francis: He was not pooling serum, he was pooling cells (and, therefore, virus) from individuals' blood, which is a very strange approach to finding a virus. You may pool things originally to see if something's there, but then you go back and dissect out the individuals, and find out from which one of them [the virus] came. Pooling is not a typical approach. As a matter of fact, we usually separate to begin with and then maybe pool later, not the way he did it.

Hughes: Why would he have pooled cells?

Francis: I don't know.

Hughes: It doesn't make sense to you?

Francis: No.

Problems with Robert Gallo

Hughes: I read that you believe that your publications and the publications of some of your colleagues were blocked after this episode with Gallo.[2]

Francis: He made it very clear that he would interfere with all of our publications. Bob may work underhanded, but he also states up-front what--in his rages, usually he will lay out all that's coming down the way. He said that we would never approve publishing anything in retrovirology from our lab. It was clear how that's done: When papers are sent out to peer review, when

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[1] See, for example, the oral history in this series with Jay Levy.

[2] Kinsella reports that papers submitted for publication with Francis's name on them were returned with mixed reviews. Since reviewers are anonymous and often give conflicting reviews, Francis could not state definitively that the negative reviews stemmed from Gallo's laboratory. (James Kinsella, Covering the Plague: AIDS and the American Media. New Brunswick, N.J.: Rutgers University Press, 1989, pp.111-112.

they're submitted to a journal, Bob's friends and Bob's lab--and Bob--would be logical reviewers for manuscripts on retroviruses and AIDS. And he made it clear to me that regardless of the scientific merit, he would obstruct publication.

So when we sent in our manuscripts, we would often get two reviews: one saying it was terrific, publish rapidly, and then making a few minor editorial comments about what needed to be done; and then a second review consisting of a three-page diatribe of how terrible the manuscript was. Ultimately, when we sent in [a manuscript], we asked the journal not to send it to anybody from Bob Gallo's laboratory. It was easier to work with after that.

Hughes: And the journals did comply?

Francis: Yes.

Attempting to Coordinate NIH, CDC, and Pasteur Institute Work on AIDS

Hughes: I understand that sometime in the spring of 1984, you attempted to set up a meeting of the NCI, the CDC, and the Pasteur Institute, with the idea of arranging a joint announcement about the discovery of the virus.[1] Can you tell me about that?

Francis: This was the early April meeting that I had described before, when we were trying to get all three of us together. It was obviously difficult with all of our schedules, but it happened that Bob was going to be speaking in Switzerland in early April, and he said, "Well, I could come back through Pasteur if you wanted," and I said, "Sure, I'll fly over." So we all met at Pasteur and discussed the various findings. That's when he excluded me from his discussions, but I laid out all of our findings, including the panel of serum that I mentioned before. It was clear that we had the cause of AIDS at that point.

The discussions were, as much as anything else, how to manage the chaos, how to come out with a single message to the public and to the scientific community that we had the virus, that the virus at Pasteur, the virus at CDC, the virus at NCI were all the same virus--we were talking about the same agent. And indeed, unstated but obvious at this point was that the

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[1] Shilts, And the Band Played On, p.435.

French had discovered it, and now we had all proved that this was the cause. We had virus in the United States--both in Bob Gallo's lab, I presumed, and certainly at CDC--that was growing from American people that looked just like the French virus; had all the same characteristics. So we were most likely talking about the same agent. Clearly, we wanted a single voice speaking here, so as not to confuse science or the public at large that was so concerned about the disease.

Part of this was selfish, wanting some sort of press management system, because the press would just drive you crazy. Reporters would call individually, and major stories could consume days. Every time there was a new discovery, it would take days just to get back to the lab and start working on stuff. So we wanted to keep each other informed and share reprints and know that we were going to have announcements coming from the different labs.

We all decided that we would publish joint papers. Bob was going to do the nucleic acid comparisons of the isolates, the French were going to do the proteins, and we were going to do the serologic comparisons. We would then come out with joint papers with all this information, recognizing that the spotlight would be on a different laboratory at different times. It was not expected that we would all be dealing with this as a group all the time; it was just too hard to logistically coordinate that. But we would keep each other informed, and we would work jointly. That obviously didn't happen.

Announcing the Cause of AIDS, April 23, 1984

Hughes: Is the next step your conversation with Edward Brandt?

Francis: The next step was the CDC press office coming to me with a press release from the National Cancer Institute announcing a press conference where Mrs. [Margaret] Heckler was going to announce that the Americans had discovered the cause of AIDS. Even though we had all agreed that we would keep each other informed about what was going on, nothing came from Gallo's lab. That was the next piece of information.

That was late in the week, and then over the weekend, Jim Curran and I--I think Jim on Saturday, me on Sunday--called Bob at home and said, "You just can't do this. This is ridiculous."

Hughes: In what sense?

Francis: That Gallo had changed the name of the virus, said that he had discovered the virus.

Hughes: Was the agreement with the French that it was to be LAV?

Francis: The final name had not been chosen, but in virology the discoverer of a virus carries considerable weight in naming it.

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Hughes: You called Edward Brandt to urge that Heckler's announcement include the French?[1]

Francis: When Bob refused to change his whole approach over the weekend, we then called Ed Brandt--I presume it was Monday--from the director of CDC's office. We all got together on the speaker phone there and said how unethical this was for Gallo to exclude the French. It would set the Americans up for future terrible criticism, because Bob was going to claim he had discovered the cause of AIDS--a new virus called HTLV-III. And we had manuscripts already in preparation that were going to say the American isolates are identical to the French virus called LAV. And how could the U.S. government explain that.

Little did we know that this was a big deal within the U.S. government. The NIH had already applied for a patent. We had no idea that that was all going on at the same time. So there were in some ways conflicts of interest here, and political desire from Reagan to do something on AIDS. He'd been criticized heavily for never mentioning it, and so having his Secretary of Health saying, "We've found the cause," was no doubt an important political advantage for Reagan's administration. With that, there was pressure on Bob and it hit Bob's weakest point, his total inability to give credit to other people unless it's within his own little club.

Hughes: How did Brandt respond to that phone call?

Francis: Brandt seemed to be very accepting of our comments, and said that he would move it up channels. It was clear that he was not in a position to make a decision without the Secretary [of Health], because the Secretary had already called the press conference. I don't know this for sure--but I think Brandt probably then inserted a line into Heckler's comments that this may be the French virus. Secretary Heckler had such a line in her written press release but never read it. She said her voice was hoarse and she couldn't carry on.

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[1] Shilts, And the Band played On, p.448.

Hughes: On the day before the announcement, April 22, there was a front-page story by Larry Altman in the New York Times.[1]

Francis: Larry Altman from the New York Times, who would come down regularly to CDC and asked us how we were doing on a variety of things, including AIDS, was actually in my office the week before.

It was very difficult for me. I had sent an announcement around CDC saying, "We have to be very careful about this information, because the primary source of this information is Institute Pasteur, and they should be the ones making the announcement and not us." I was saying exactly the opposite of Bob Gallo, and I was giving individuals advice on how to deal with the press, saying, "Well, we've got some information about the virus; it's not proven yet." You didn't want to lie, but you didn't want to fan the flames of public excitement until the Pasteur had announced.

So Larry Altman came into my office, and he never asked me the right question. He said, "How are things going?" And I said, "Fine. We're getting some interesting information." He didn't ask more. And I never said a thing. So I think Larry left thinking this is all rather dull, but then went up to Jim Mason, the director of CDC, whom I had briefed on all the data concerning LAV. And for some reason, Jim just opened up. I guess Larry asked Jim Mason the right question. Jim Mason just opened up and gave him all the information.

But by this time, we had had word that NCI was going to make an announcement. So Jim Mason asked Larry Altman not to put the article out until after the NCI announcement, so it didn't look like we were trying to steal any credit for the work that NCI was doing. Larry didn't know what that meant until he got a copy of the press release. He told me he called Jim Mason and said, "I'm sorry, I have to violate our understanding about this, and I'm going to go ahead and publish the article now." So I think he put it out in the Sunday edition of the New York Times.[2] Gallo saw that as a clear move by CDC to try to undermine him, and further fanned his paranoia.

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[1] Kinsella. Covering the Plague, pp. 83-84.

[2] According to Kinsella, the New York Times ran a front-page article stating that James Mason believed LAV to be the cause of AIDS. (Kinsella, Covering the Plague, p. 83.)

Hughes: I am assuming that your main problem with all this is where credit should be laid. But is there also a concern about publicizing science before it has appeared in a peer-reviewed journal?

Francis: No, not at all. I think that's nonsense, this waiting for peer review. That's a New England Journal, try-to-sell-magazines, thing. If you're confident about your science and it has important public health information, you should never wait to announce it. That's just garbage. If the New England Journal doesn't want it, then screw them. Don't even give the paper to them.

Controversy and the AIDS Research Community

Francis: The issue was not just on the credit. The issue, in a public health sense from my standpoint at CDC, was giving the message to the public that we had the cause and we were moving ahead. We certainly didn't want the message to be that we had two causes. It was horrible. And what it did, which I don't think I saw coming--I probably felt it, but I didn't think it would be so bad--was you ended up dividing the whole relatively small virology community now working on this bug into two camps: one which had to collaborate with Pasteur, and the other one had to collaborate with Gallo. It was very hard to walk those two lines, because Gallo said, "Work with me and not them." So the relatively small world's effort on AIDS was divided. To be effective in this field you need collaboration, sharing reagents and resources and information.

Hughes: And the division got worse over time?

Francis: Oh, for the next year and a half, two years. And to this day, it's still there. To this day! It's less now, because there are a lot of labs working on AIDS, and they don't need Bob Gallo or the Pasteur. So they can go on their own.

Hughes: But you did need Gallo in the beginning.

Francis: Oh, we all needed each other. The divisiveness set AIDS research back years. This guy was a paranoid, childish fellow who could not share credit and undermined the whole AIDS field, for years and to this day. Here we are, spending national resources investigating his lab, going over his records, having testimony and lawyers coming to talk to me and all this stuff. If he had just been an honorable person this would never have happened, and

the resources would never have been wasted, not only inhibiting science in its collaboration to advance prevention and treatment, but all of the other spin-offs and nonsense that came from it.

Hughes: Do you think it also deterred people from entering the field?

Francis: Sure. There were people who called me who were very good virologists--and asked, What was the field like; what about Gallo? We needed virologists in this endeavor, not just cancer virologists who dominated the field early on. We needed people who were working with horizontally transmitted viruses, which most retroviruses are not. It was only Max and Bob and myself and a few others working on these horizontally transmitted ones. We needed these other people in the field.

Hughes: You were working on horizontally transmitted retroviruses?

Francis: Feline leukemia virus is a horizontally transmitted retrovirus.

Hughes: But you were also seeing horizontal transmission in the field. Right?

Francis: Right, for AIDS from person to person, not from the mother to infant.

Hughes: Why wouldn't everybody have seen that transmission could be horizontal?

Francis: I think by that time they ultimately did. There were still people harping about other causes. But what I'm talking about are people with experience only in vertically transmitted retroviruses now having to work in [the field of horizontally transmitted viruses]. We needed broader experience. But they stayed out of it, because the field was ugly. Why would you want to work in an ugly field?

Hughes: And the money for AIDS research wasn't there yet.

Francis: No, you had to sacrifice your existing grants and/or work.

Hughes: In her press announcement, Heckler made some predictions that since have proven very wide of the mark. On what basis did she predict that a blood test would be available in six months, and a vaccine in two years?

Francis: I have no idea. I presume some of it came from Bob Gallo, but I don't know.

Hughes: What did you think, once that you had the virus?

Francis: Well, those were a bit overly optimistic predictions. But I probably would have predicted optimistically too. I don't know if it would be those exact ones. I never thought about it really. I think I'd probably be a little cagier; I don't think I would have put the date right on it. "Soon we will have..."

Gallo, HTLV-III, and LAV

Francis: There's etiquette that the first person who isolates a virus has property, and you have a responsibility as a scientist working with a virus to compare your isolates to those which predated yours. That's where Bob fell down; he did not want to compare his virus to the initial French isolate.

Hughes: Why?

Francis: We took our isolates from Americans and compared them to the French, and found out that they, by several techniques, appeared to be identical. I discussed that with Bob over the telephone, saying that the viruses that we were growing from Americans were identical to the initial French isolate, so the French indeed had discovered the virus first. If Gallo had made that comparison, then he would be admitting that he did not discover it first. If he didn't make the comparison, it looked as if he discovered it--at least for a time.

Hughes: Does that explain a lot of his subsequent behavior?

Francis: Sure.

Hughes: Not willing to give out the virus--

Francis: Gallo's policy was, "Let's not give it out"--at least to the CDC.

We ultimately got the virus from him, but he forbade us to compare it to anything. That was one of the rules. Murray Gardner at [University of California at] Davis here compared the virus, and was told that he was not allowed to publish that research, because that was Bob's responsibility. Gallo's nomenclature, HTLV, was actually human T-cell leukemia virus, but he had adjusted the name to "lymphotropic" so that it would fit both with his initial HTLV-I and HTLV-II, and now what he called HTLV-III.

But it was clear at that time--the electron micrographs were--this [the virus causing AIDS] was a different virus. This

was not a retrovirus like HTLV-I, like HTLV-II. This was a lentivirus, which was a different subclass of retroviruses. So it was a different agent.

Hughes: How could he not see that?

Francis: He admits to me that he did not look at the electron micrographs. He didn't really think that that was important to him.

Hughes: Even the ones that he himself had produced?

Francis: Yes. As came out in the future, the ones that he actually published in his manuscript were not of his virus but were of the French virus.

Hughes: Yes. I suppose you've seen that amazing report from a contract lab where he had sent virus specimens.

Francis: Yes, from Matt Gonda, who did the EMs [electron micrographs].

Hughes: Right. The purged version has a gap where information about the LAV specimens had been deleted.[1]

Francis: Yes. As I understand it from those investigating his lab, there were many of those kinds of "adjustments" where, despite denying it, they really were growing LAV. Then they changed the name [of the virus to HIV].

The Effect on Science of Identifying the Virus

Hughes: One more question on the isolation of the virus. Research shifted to a reductionist, bench-science approach once the virus was isolated, where before it was a broad, epidemiological approach.[2] What was gained and lost in the process?

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[1] Gonda indicated in the original report that electron microscopic pictures of only samples 6 and 7 showed a retrovirus. These samples were labeled HUT78/LAV and T17.4/LAV. Clearly, Popovic's cell lines were infected with the French virus. The notations concerning the two samples were absent from a subsequent copy of the report. (Grmek, History of AIDS, p.76.)

[2] Gerald M. Oppenheimer. In the eye of the storm: The epidemiological construction of AIDS. In: AIDS: The Burdens of History, Elizabeth Fee and Daniel M. Fox, eds. Berkeley: University of California Press, 1988,

Francis: Well, I was in charge of a laboratory, and it was epidemiology that directed my laboratory effort.

Hughes: You're unusual in that regard.

Francis: Well, that's the way it should be done. I had three Ph.D.s who were assigned from other fields, and about the same number of technicians. You can't do everything with that size of a laboratory, and so you have to narrow it down. Data made it very clear that we were talking about a horizontally transmitted agent. After the hemophilia cases came forth, the agent was [concluded to be] a virus, because plasma was filtered to filter out everything bigger than viruses.

Recognize that there were still lots of viruses [being considered as the possible cause of AIDS], which was a problem. We had other laboratories at CDC looking at whatever they were best at. But all results to date indicated that this bug was new. From our work with the other viruses, nothing panned out, so we were talking about a new agent that probably multiplied in lymphocytes. So that brought us down to a few types of bugs.

Once we had the virus, then a huge amount of information could be gained. We had planned all of our epidemiologic studies with the assumption that we were going to have a virus and a test--eventually. We had all our specimens characterized and in systematized freezers, so when we wanted specimens from a bunch of gay men, a bunch of gay men with AIDS, a bunch of gay men with lymphadenopathy, we wanted transfusion cases, et cetera, we could pull those panels out. Once we had a test for infection, we could go back to our frozen specimens from San Francisco and figure out exactly what proportion of people came down with AIDS with time. We could get samples from gay men in San Francisco, Denver, Chicago, and find out how long ago this virus had been around, and how much damage was done.

Next we could get all the epidemiologic data of how the infection spread. We could move into families and see if it spreads within families. We could get all this important information fast. Recognizing that we had a disease that what we knew at that time had a three- to ten-year incubation period, for an accurate epidemiologic picture, we needed to use the HIV antibody test to tell us where the disease was going. You can't use AIDS, because that's like driving your car with the rear-view mirror; you see what happened ten years ago. So the test was an

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pp.267-300.

incredibly valuable tool that really outlined the epidemiology of AIDS worldwide.

Hughes: The commercial test wasn't available until March 1985.

Francis: But we had to manufacture our own [antibody test], which was a pain in the butt.

Hughes: How long did that process take?

Francis: Within a few weeks of getting the virus from Jean-Claude.

Hughes: Why was it a pain in the butt?

Francis: Growing large volumes of viruses is a laborious process. Instead of going out and buying a kit, you've got to grow the virus, purify the virus, get it onto a plate, control the plates, be sure they work, run them all, run your tests, and then grow some more virus. We ended up having to dedicate one or two technicians just to do that, and I didn't have that kind of staff.

Hughes: But the technology was all there? You didn't have to invent it as you went along?

Francis: No, no. Once you have the virus, you can just plug it into existing technology.

Hughes: Which was the ELISA [enzyme-linked immunosorbent assay]?

Francis: Yes, together with others.

Hughes: Is that obviously the way to go?

Francis: Sure.

Hughes: What about the Western blot?

Francis: There are several other alternatives you could use for confirmation, either the Western blot or fluorescent antibody, or we were using RIPS [radio immunoprecipitation]. Everyone was using different methods for confirmation. For some reason, Bob [Gallo] liked the Western blot, and the U.S. government in Washington got behind the Western blot. But it was probably the most expensive, difficult thing with a new technology out there, to be honest. It's okay. But the California state lab still uses fluorescent antibody, which is much cheaper. It's just a different way to look at it.

Hughes: Why Western blot, then?

Francis: I don't know. There was a guy named Lowell Harmison making policy from high levels of HHS [Department of Health and Human Services]. He declared the Western blot to be the standard.

Hughes: So you had the test. What did it show you?

Francis: Because we had limited resources, it took us months to generate all the data. As I said, I had to go into the freezer and actually sort the specimens myself, because we didn't have anybody else to do it. But despite the limits, the data came rolling in; we showed that the virus had come in to San Francisco somewhere around '78. There was relatively low prevalence until about 1981-1982, and then it shot up, infected half to three-quarters of our cohort.

Hughes: This is the hepatitis cohort blood?

Francis: Yes, but see, we had cohorts in St. Louis, Chicago, and Denver, so I went back and pulled specimens from them too. We showed 20 percent HIV antibody prevalence in those cohorts. So it was all over the United States. Already 10 percent of infected cohort members in San Francisco had developed AIDS. Now, that was really high. That showed us that at least 10 percent of the people who got infected with this virus developed a fatal disease.

Hughes: Is that unprecedented?

Francis: There aren't very many human or nonhuman viruses--Lassa, Ebola, smallpox--that produce such high rates of fatal disease. It gets up to about 70 percent fatality with Ebola, and then rabies is the top with 100 percent, and then HIV sits right up there. Now, recognize that neither rabies nor Ebola are human viruses; they're non-human viruses that dead-end in humans. Usually viruses that kill that proportion of individuals don't do well epidemiologically, because they burn themselves out. HIV, it's just more clever in that it has a long incubation period--all the virus has to do is infect one other human before that human [the original host] dies, and then it will stay alive.

The Blood Banks and Blood Screening

Irwin Memorial Blood Bank and Hepatitis B Core Antigen Screening

Hughes: How long does it take to develop a vaccine, once you isolate the virus?

Francis: Years. Decades, usually. It takes a long time. That prediction by Secretary Heckler was overly optimistic. You should never come down with that kind of a prediction for a vaccine. A blood test was a little easier.

Hughes: Well, the prediction for a test was close.

Francis: It was six months off. And it hurt. The blood banks needed a sense of urgency to screen out at-risk donors. They never had much, and that prediction of a test around the corner just took any urgency that they did have totally away. So they said, "Well, we'll have a blood test in six months, so we don't need to think about screening donors any other way." And that killed another 5,000 people.

Hughes: Irwin started hepatitis B core antibody testing before the test for HIV was available.[1]

Francis: Irwin did, and all the Bay Area blood banks did.

Hughes: Are they the only ones?

Francis: Yes, for anti-core [hepatitis B antibody testing]. But that wasn't because they were interested in protecting recipients; it's because they got pressure. Stanford was screening donated blood with T-cell counts a year before [May 1983].[2] The doctors and patients in the Bay Area were suddenly saying, "There are two classes of blood here." That's really important: Irwin did not

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[1] In May 1984, Irwin Memorial Blood Bank [IMBB] implemented hepatitis B core antibody testing as a surrogate test for HIV in donated blood. (IMBB AIDS documents, binder 2a.)

[2] Edgar Engleman, medical director of the blood bank at Stanford University Hospital, screened blood donated at Stanford with the fluorescent-activated cell sorter to obtain helper-suppressor cell ratios. If the ratio was abnormal, he discarded the blood. (Shilts, And the Band Played On, p. 308.)

want to screen blood for hepatitis B. They did it because UCSF doctors were complaining they were losing their patients to Stanford. Irwin dragged their feet as long as they could, and finally were forced to do it, as they say, for political reasons.

Hughes: You're absolutely right: UCSF was losing patients to Stanford. But Stanford didn't institute the hepatitis B core antibody test.

Francis: No. The January 1983 meeting mentioned five blood-screening tests blood bankers could use, or if you really wanted to be compulsive, combinations of those five tests, T-cell tests being one of them, and the hepatitis B tests being two others. Engleman chose T-cell testing. As a matter of fact, Ed Engleman admits he didn't know anything about anti-core, because he never got the information from the blood bankers who attended national meetings where we presented the data. They chose to keep that information about anti-core away from the folks in the field. Ed happened to have that very expensive machine [the cell sorter] to do T-cell tests, so it was relatively inexpensive for him to do it, and he just did it. He was not at the meeting, but he got the idea from an announcement about the meeting. But he never saw the data about T-cells versus hepatitis B or any of the other tests.

Hughes: Of course, he had an advantage in having a cell sorter, which most people did not have.

Francis: Oh, yes. It was $100 thousand, and it would probably take a year to order [and receive] one. He just happened to have one on the other side of his wall.

Hughes: Is the presence of the machine related to Stanford's organ transplantation program and the fact that it needed large amounts of blood?

Francis: And the fact that it was a big research institution. If you wanted to be on the cutting edge of research on surface proteins of blood cells, you needed a cell sorter. So Stanford had one.

The January 4, 1983 Meeting at CDC on Blood Safety

Hughes: I know you had some very firm things to say at that January meeting [Workgroup to Formulate Recommendations for Prevention of Acquired Immune Deficiency Syndrome], which followed Art Ammann's

baby, the December 1982 death of the transfusion baby who was then linked to a donor with AIDS.[1]

Francis: Correct.

Hughes: Tell me about that meeting.

Francis: Oh, it was a horrendous meeting. In many ways, we [CDC] were hoping to move the responsibility for preventing blood infections off to the FDA and the blood banks and the plasma collectors. Because frankly, blood transfusion was responsible for only 2 percent of our total cases of AIDS, and we had 98 percent of the cases, and we had no resources to deal with those. So anyone that would help was welcome, including Bob Gallo or the blood banks. Early on with the IV drug users coming down with AIDS, we were very suspicious that there was a problem with blood. The hemophiliacs with AIDS came forth in the summer of '82,[2] and we had the initial meeting with the plasma collectors in Washington D.C. in July of '82.

Hughes: The commercial plasma collectors?

Francis: Yes.

Hughes: They were receptive to your suggestion to screen blood products?

Francis: Some were certainly more receptive than the blood bankers. This was interesting because they were always viewed as the low-class group of blood collecting, because they're commercial and they're seen as sucking plasma from poor people.

Hughes: Why do you think they were more receptive to screening?

Francis: I don't know. There were some people who saw the problem, at least at Alpha Therapeutics. A guy named McCurdy, I think, and Drees were the two that made that decision.

Hughes: Could it be that they realized that business would obviously be hurt if the word got out that plasma was tainted?

Francis: You would certainly think so. You would think that the free market should have led the way on this, and the competition

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[1] For details, see the interviews in this series with Arthur J. Ammann, M.D., the UCSF pediatrician who handled the case.

[2] Pneumocystis carinii pneumonia among persons with hemophilia A. Morbidity and Mortality Weekly Report 1982, 31:365-367 (July 16, 1981).

between the various companies for a better product should have increased positive action. But competition for safety didn't last long.

By November of 1982, we at CDC were worried enough about blood to publish precautionary steps for hospitals to take to prevent health care workers from coming down with AIDS.[1] We figured that if it was blood-borne, the next folks to get it would be health care workers.

Hughes: What were those precautions?

Francis: They were basically hepatitis B precautions with blood, caution dealing with blood and labeling of blood from patients, alerting the lab, alerting the clinicians to be careful. Realize that there were no cases of AIDS in health care workers at that time. But we in public health thought that we should act in advance to prevent it.

By the January 1983 meeting, we had Art Ammann's baby and five other cases of blood transfusion AIDS in adults around the country. The investigations of these cases had shown--those that were completed--that a gay man donated a unit of blood in each of these cases. In the one case in San Francisco, the donor had already developed AIDS. The rest of the suspect donors were healthy. So then the issue was, how to eliminate blood from gay men from the donor and plasma pools? Already IV drug users and Haitians (other groups at risk of AIDS) were supposed to be excluded. But they were not big blood-donating groups anyway. Gay men were not excluded but needed to be.

Resistance from Blood Bankers

Francis: Initially (at the January 1983 meeting) the blood banks refused to accept this possibility of blood-borne AIDS. They were willing to accept plasma-borne transmission, but were unwilling to accept blood-borne. That's a little bit like saying, "Well, you can get in an automobile accident with a Ford, but you can't get in an accident with a Chevy." It just made no sense whatsoever.

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[1] CDC. Acquired immune deficiency syndrome (AIDS): Precautions for clinical and laboratory staffs. MMWR 1982, 31(43):577-580 (November 5, 1981).

They said, "Oh, you guys at CDC who are concerned about transmitting AIDS through blood don't have enough data." As the year went on, there were memos by blood bankers where they were trying to push CDC out of their hair. In reality, CDC was perfectly happy to be out of this field, but we wanted to have some public health action before we would release all responsibility.

There were memos from blood industry leaders wanting to get FDA and NIH more involved in this and CDC less involved. There was even one memo saying that CDC was using this epidemic to generate resources for CDC [de Banfort, Red Cross]. I mean, it was just the most amazing stuff I've ever seen. [laughs] The CDC needs more money, so they're manufacturing this epidemic? These guys [blood bankers] were the most status quo, inertia-seeking people I've ever met in my life. It was very frustrating.

And the FDA was clearly not going to move. Dennis Donohue was head of the FDA blood products division [director, Division of Blood and Blood Products, Office of Biologics, Food and Drug Administration] at that time. He was just this slow-moving, let's-all-work-together type person, and he was not going to exert the FDA autonomy and say, "Do it [anti-core hepatitis B antibody testing]."

Hughes: You make it sound as though that was just his process, but was it more than that? Was he getting pressure from the blood bankers?

Francis: He was a blood banker.

Hughes: Ah.

Francis: Very recently, he had come from the blood banking field up in Seattle. I don't think he really understood his new responsibility when he changed hats. You can imagine the personality of a blood banker. These are not change agents. These are SOP [standard operating procedure]-following people; let's make rules and follow them day in and day out exactly the same. Which is what you need to manage a blood bank. I didn't understand this at the time that we at CDC were epidemic-chasers, and we were changing things all the time. We were perfectly comfortable as agents of change. Blood bankers, when it comes to change, get very nervous. We said, "Well, they'll change, just give them a few more weeks or months." And they never did. I've seen afterwards all the information that's become available through litigation on this issue. What they were doing behind the scenes was just unbelievable--just unbelievable!

Hughes: Such as what?

Francis: They went out of their way to kill people. They would make these public announcements of "one in a million risk [of getting AIDS from a blood transfusion]," and "I don't know if there's such a thing as transfusion-associated AIDS," and they would minimize the whole thing. And yet, behind the scenes, they would write these memos saying, "Well, I think there really is such a thing [as blood transfusion AIDS], and we're probably going to have to start screening donors, and we'd better change this, and we'd better think about anti-core testing, and better evaluate it." And they didn't do anything. They just kept this, "It's all fine; don't worry about it," facade--you can talk for hours of why. It makes no sense at all.

Hughes: What was the main argument blood bankers were putting forward?

Francis: Donor screening and donated blood screening were going to cost money and lose donors. Herb Perkins summarized it best, if you get the transcripts of the December 15 or 16 Blood Products Advisory Committee meeting in 1983. At this meeting--now a year after the January meeting--participants were talking about anti-core testing. Herb Perkins said, "Well, I think it's a great idea, except that it costs money, causes trouble, and we have to tell patients--it causes concern in patients if we have to tell them they're hepatitis B infected." I mean--it was trouble.

Hughes: Dr. Perkins would argue, I believe, that as a blood banker, his primary responsibility was to ensure that the nation had a supply of blood.[1]

Francis: That is absolutely true, and absolutely garbage when it comes to an excuse for causing transfusion-associated AIDS. These guys were on the front page of Newsweek. If you wanted to change the entire donor pool to all women with family incomes greater than $50,000 a year, you could have done it. You would have had women lining up a mile long around the corner of blood banks if they wanted to use the media who were sitting there knocking at their door. Instead they said, "Ah, no problem, one in a million, don't worry about it. Now let's go out and put our effort into recruiting donors." Six percent of Americans donate blood. That leaves 94 percent that you can tap into, and when you've got Newsweek at your door, it's not hard to do that.

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[1] The statement is based on the oral history in this series with Herbert A. Perkins, M.D., in process.

When the blood banks ultimately did anti-core testing, there was not excess trouble getting blood donors. The American public will rally for that kind of thing [and donate] more blood than the blood banks can take. That was an excuse to do nothing.

Hughes: And you think that's what it was?

Francis: I think they wanted to avoid trouble. It was trouble to get new donors. They would have to say, "We need new donors," and all the telephone calls would come in, "How do you get AIDS?" It was trouble. They weren't willing to put up with that trouble to save people's lives. You've got to recognize that the blood banks deal with the donors. We dealt with the recipients. They don't see the recipients with the disease; that's the doc's problem, and it's public health's problem when they get hepatitis or AIDS. So their issue really was donor interaction, keeping their donors happy and keeping their staff in the blood banks happy. And to hell with the poor people who received it. [tape interruption]

Hughes: Anything more on that hot subject?

Francis: It's endless.

Hughes: Are you still testifying in the transfusion AIDS cases?

Francis: Yes, as little as I can. I could do it seven days a week, and it's just not what I want to do for the rest of my life. I've really urged the blood banks to settle, but it's such a huge problem, they're just kind of holding off, waiting for it to go away. And it will. It will go away, and these orphans will be left without parents. I've seen cases where the father gets infected via transfusion. He infects the mother, and then they both die. Only the kids are left. It's a sad chapter in health history, and I think we've got a long way to go to improve that so it doesn't happen again, because I think it could happen tomorrow.

Governmental Responsibility

Francis: When it comes to governmental responsibility--you have to be careful not to have too much government, because if you do, you cost the society in lost resources and lost spirit. But we do need government in some areas. With AIDS the Reagan administration totally lost the understanding of what government (public health) responsibility was to the people. These blood

banks would have been happy as can be to do anti-core testing and direct questioning of donors if the FDA had said, "Do it."

It's good to work in a collaborative way with the groups that you are regulating, but there's a limit. And that limit is when the public's health is jeopardized, and then you've got to move fast. You've got to pull those cans of contaminated soup off the market. It's usually done voluntarily. Look at Tylenol. There, there was a crazy person in Chicago putting cyanide in pills, and [the maker of] Tylenol at a huge expense pulled all the pills off the market in the United States. Now, that was probably overkill, but they did it because they had a responsibility. And the FDA didn't have to say anything.

Some of these guys in the Reagan administration were jerks. They were just jerks. They had some right-wing, conservative ideology, extremism at its nth degree. The word seemed to be, "Let's ignore as much as we can now and later there will hopefully be another administration in government and we won't have to worry about it." Meanwhile, a million Americans die. The blood banks alone infected somewhere in the neighborhood of 28,000 Americans, and the factor VIII folks another 10,000.[1]

Over half of transfusion recipients die from their underlying disease, so that leaves about 10,000 to die of AIDS--plus 10,000 hemophiliacs. That's 20,000 Americans. If you're driving around in your car and you're not looking and a kid runs out in front of you and because you were looking the other way you kill the child, you go to jail for that. For one death. And here you've got 20,000 people who are killed, of whom easily half, if not three-quarters, were preventable. And now we're wondering whether we should change our blood donation system or not. It's very strange.

We have to change things and make damn sure it doesn't happen again. Unfortunately, it's people. If you recruit status-quo-seeking people, you will get the status quo. And if you don't make jobs in government exciting and fun and responsible and prestigious, then you'll get the status-quo-seekers who can't find a job anywhere else.

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[1] T. A. Peterman, H. A. Jaffe, P. M. Feorino, et al. Transfusion-associated acquired immunodeficiency syndrome in the United States. Journal of the American Medical Association, May 16, 1985, vol. 312(20):1293-1296.

T. A. Peterman, D. P. Drotman, J. W. Curran. Epidemiology of the acquired immunodeficiency syndrome (AIDS). Epidemiologic Reviews, 1985, vol. 7:1-21.

Hughes: Do you take some heart with what's happening in the Department of Energy now, with the release of the information about the plutonium victims?

Francis: Yes. I think I take heart with this new [Clinton] administration. But there's a lot more than that that needs to be done. You just can't come in with a president and change this whole bureaucracy. It has to be a philosophy, a fundamental policy of the government that it is going to be sleek and efficient. We must realize that government cannot be as efficient as the private sector, because its funds are not its own. It runs on someone else's money. So there's going to be more accounting, and it's going to be slower to move. But it's got to be as close to first class as we can [make it], instead of fourth class.

Hughes: The Constitution says nothing about assigning public health powers to the federal government, and the way our system works, that means the states have the responsibility. Was the Reagan administration playing that to the hilt?

Francis: Yes. I was paid, and a half dozen other docs, a full-time salary to work on one virus. That's at the federal level. Most states cannot afford that level of specialization. When states require that level of expertise, they turn to CDC for guidance. It's worked quite well--in the past.

Sometimes CDC puts the screws to a state government to improve their programs--

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Francis: --if it's CDC money paying the bill. And then if the state doesn't do a satisfactory job, CDC pulls its money out. In general this collaboration can work extremely well. But you must have first-class federal public health employees. Recognize the size of the budgets we're talking about here. When I was in Atlanta, Massachusetts General Hospital, one hospital in the United States, had the same budget as CDC and CDC had the same budget as WHO [World Health Organization]. So you're talking about small amounts of money. I think at that time [1983], CDC had a $700-million-a-year budget. For a country this size, the people get a huge return in health--not to mention worldwide benefit. When an organization works collaboratively with other organizations in the world and wipes out smallpox from the world, the money that you get back year after year on that is immense. Same with measles and polio, and whatever. Just a huge benefit.

But we as a society are not mature enough yet in a social evolutionary sense to realize it. It will take time.

AIDS in Africa

Hughes: When did AIDS in Africa affect your thinking?

Francis: Early. You'll have to ask Joe McCormick whether word of African AIDS first came from Europe or whether he heard it from Zaire. Whatever the source, Joe and his team were off to Africa to discover AIDS. CDC had had a long history of working with west Africa with smallpox and many others diseases. The Belgian cases, I think, were my first knowledge of AIDS in Africa. Now, others may have heard about it elsewhere. But the Belgian cases of AIDS were from Africa, including Zaire. Very early on, we sent a team over to Zaire--

Hughes: Can you think of the year?

Francis: Late '82, early '83. Joe McCormick went over. Joe was the head of the hot lab, the Lassa-Ebola lab, at CDC. He was actually a high school teacher in Zaire years ago before he went to medical school. He was close to Mobutu, got in the country, brought a team over--Peter Piot from Belgium, Joe McCormick from the United States, a couple of others from the United States, and maybe some others from Europe. They came in and did an investigation there, which was published in Lancet. A two weeks survey at Mama Yemu Hospital found forty, fifty cases of AIDS or something like that. It was incredible. So even early on it was already a big problem in Africa.

Hughes: Now, what about the heterosexuality of the disease there?

Francis: It was obvious from their investigation. The number of men and women were almost equal. But the female cases were younger; the male cases were older. Many of the females were femmes libres, "free women" who worked in bars and were sexually very active. And the males were their customers.

Hughes: Did knowledge of the heterosexuality of the African disease affect your perception of the disease in this country?

Francis: Well, the earliest were the Haitians in this country, which brought a tropical nature to it. The issue of the Haitians was confusing, though, and wasn't sorted out for years, actually. We knew that gay men from New York were commonly coming down to

Port-au-Prince for vacations, and hiring local youths for sex. Haiti had a very close connection to Africa, and indeed Zaire, because post-colonial Zaire needed school teachers and imported Haitians for that. The question was, did it come into Haiti and then get into the gay population through Haitian interaction with gay men in New York, or were the Haitian cases a result of gay men who were infected giving the virus to Haiti?

The latter turns out to be the case, but initially we thought that an African bug went to Haiti and then got into the gay population. Obviously, it probably was an African virus--gay men visiting Africa picked it up and got it into the bathhouses in Europe and the United States, and then it spread like crazy.

Early Perceptions of AIDS

Hughes: What I'm trying to get at is, the early perception of AIDS is linked with the gay population. It is seen by most people as a gay disease.

Francis: No. When we see a disease in the gay community, our initial instinct is that it is infectious, that it's sexually transmitted, not that it's a gay disease. So the assumption, I think, of all of us at CDC was it's just a matter of time before it spreads out [into the general population]. Gay men were the flagship of any sexually transmitted disease. We knew that. They were always the leaders, because of their numbers of sexual partners.

Hughes: Did you find that to be a common perception?

Francis: Yes, at CDC.

Hughes: Beyond CDC?

Francis: I think it was a common perception of anyone in the infectious disease field who was experienced. Some of the researchers who never put it all together would proffer their sperm hypothesis or their immune overload hypothesis and all that dribble, but we just kind of chuckled at them. We'd try to bring them around, and they wouldn't come around necessarily, but we let them do their thing.

At the January [1983] meeting on the safety of blood and products, Dave Sencer, who was the health commissioner of New York City, said, "Is there anyone who doesn't believe this is

infectious?" And Don Armstrong, who is an infectious disease doc at Sloan-Kettering Memorial Cancer Center, said, "I have no doubt that this is caused by an agent; we've got to go out and find it." This was not magic; anyone who took ten minutes to learn the facts would conclude it was infectious. A lot of people didn't spend the ten minutes, that's all.

Risk Groups

Hughes: What is the implication of identifying risk groups, both for you as a scientist and also for the public?

Francis: You have to be scientifically accurate when you're describing a disease. When we're describing the epidemiology, as we did for hepatitis, we interview patients and ask what behavior these people have that would put them at risk--having a child in a day care center, having sex, sharing needles and syringes, eating a picnic, or whatever it may be for the given disease. We classify cases by their risk, and have for years and years and years, and continue to.

For AIDS, the behaviors associated with infection were: gay sex, sharing intravenous injecting equipment, and there was heterosexual sex, and being born to a mother who was at risk. Those risk categories by and large haven't changed at all, except for adding transfusion [cases] and hemophiliacs to them. All that was cooked [up] in late 1982, and very little has changed.

Now, the problem that we had in a public health sense and a political sense was, instead of talking like an epidemiologist who talks about a risk group, it was important for society to talk about risk behaviors. Inappropriate use of the "group" terms seemed to stigmatize people. The Haitians were the ones who ate it early on, because indeed it was not all Haitians. It turned out to be recent Haitian immigrants who prostituted themselves for gay men (or their sexual contacts).

But there is stigmatization that can come with any epidemic. In public health we're always cognizant of the potential and try to minimize it. But we recognize that sometimes to save a lot of people, others may be injured. To prevent AIDS we needed to talk about men as a group who were having sex with other men. The message was, if you have sex with other men, you are risking AIDS. That was a very important message to get out. The gay community didn't always like it, because if you were a monogamous gay man who had only had sex with your partner, and your partner

had only had sex with you, or if you were gay and you never had any sex at all, you didn't have any risk. And that's true. But that's a much more complicated education message to dispense. What you need to do is break the ice with these sometimes potentially stigmatizing messages, and then refine your educational program with time. But if you try to refine it at first and try to prevent all stigmatization, you'll take all the bite out of your message, and no one will ever get educated.

The Behavioral Approach to AIDS Prevention

Hughes: Well, the idea of the risk group has been criticized for taking emphasis off behavior. It also lets people off the hook who don't fall into those risk groups; they can divorce themselves from the problem of acquiring AIDS.

Francis: Yes. And the issue is behavior. There's no doubt that why gay men are infected is a mathematical issue. I think maybe anal sex has a little bit more risk than vaginal sex, but to the woman, or the receptive male partner, it's not that great of a difference, to be honest. So it is receptive sexual behavior that's going to get you into trouble. And yes, that is important to get over, and you have to be very careful about dealing with behaviors.

But frankly, we in public health were pretty naive on all of this. Most of us were not behaviorists; we were vaccinologists. We were people dealing with penicillin shots. We're talking about one or two visits to prevent disease for a lifetime. That's about the extent of public health's reach out in the world. Sometimes we can't even do that. Often we can't even get people immunized in this country with one, two, or three visits. So we're accustomed to working at a relatively simple level. But when it comes to behavior change, far more sophistication was needed.

It was a new field of chronic disease epidemiology and prevention, as it was called, and we luckily had some of those people at CDC and could tap into them, but they were a very small group. So you basically had Jim Curran, Harold Jaffe from sexually transmitted diseases, and myself. We were one shot of penicillin and a follow-up visit, which meant two shots-of-vaccine people.

Hughes: [laughs] Then your problem's solved.

Francis: Then the problem's solved. And for smallpox, it was only one shot.

Hughes: Was it hard for you to realize that you had to take a different approach to this epidemic?

Francis: Yes, it was a different approach. I think we were naive about it. When I came out to California, I just luckily, with Marc Conant's and Jim Chin's help, was introduced to people who knew what they were talking about.

Hughes: From a behavioral standpoint?

Francis: Yes. I got to know Larry Bye and Tom Coates and Steve Morin--these are behavioralists. I sat down with them at a variety of lunches and dinners and had them try to convince me that there was such a thing as changing behavior, and they convinced me. Steve Morin and Tom Coates and Leon McKusick did some of the earliest studies of gay male behavior. And what proved to me that gay male behavior could be changed was their saying: "We went into this group assuming, from our smoking research information, that these parameters would change people's behavior: recognition of risk, self-motivation, and feeling that you could do something about it, having some empowerment. And we asked questions to quantitate these parameters.

"We had in gay men a group who altered their risk-taking behavior and a group who didn't change, and we asked the questions of both groups. At onset they predicted factors, say, one, two, three, and it came out to be one, three, two." It was incredible. I was convinced. I was sold. Now the question is how to market that message to the general population, and that's where people like Larry Bye and Tom Coates were superb.

So do we have the answers as to exactly how to change human behavior? No, we don't have all the answers even today. But we have an awful lot of groundwork that was already there from other research, and now we have a good deal of AIDS-specific research to direct our "best guess" program design.

Hughes: In the gay population, you have generally well-educated, well-motivated, politically astute people. The epidemic is moving into populations which don't have those characteristics.

Francis: The gay community is diverse. And you've got to realize in the gay community, there was tremendous resistance, too. This was a new political movement that had come out of the closet, and anyone who talked about decreasing sex was anti-political. It was against the movement. Randy Shilts and an awful lot of other

folks were seen as wanting to close the bathhouses and change gay behavior. And certainly I was seen as an outsider. "What right do you as a straight man have in advising us about our sex? All you are is a messiah from Ronald Reagan saying, I want to stop all this anal sex stuff." Realize I was saying, "You better stop that anal sex stuff." So it was a very easy take.

AIDS in Women and Children

Hughes: Another criticism that the CDC has suffered is its reputed delay in recognizing AIDS in women and children, and failing to incorporate those populations in the case definition of AIDS.[1] What do you have to say about that?

Francis: I don't think so. I'm sure CDC can be criticized, but CDC recognized and reported women very early on, and the risk was recognized as being huge.

Hughes: Yes, but the case definition of AIDS did not embrace symptoms specific to women.[2]

Francis: That was nonsense. That issue was, who was going to pay for AIDS treatment, which was not the purpose of CDC's AIDS definition. The definition very soon should be [simply] HIV infection. If it weren't for political pressure against it, it would be. Money was the issue. In contrast, the several symptoms were an issue of what disability payment one received, what kind of medical care you required, et cetera. And unfortunately with this primitive system we have in this country for paying for medical care, people were using the CDC case definition to decide whether the government would supply medical care to them. CDC never meant to get into that.

Hughes: And it hasn't historically?

Francis: It hasn't historically. It's a little easier historically, if I have polio, if I have hepatitis. They're easier than AIDS [to

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[1] The inadequacy of the federal government's response to AIDS in women is a theme of Gena Corea's The Invisible Epidemic: The Story of Women and AIDS. New York: Harper Collins, 1992. For discussion of resistance to the idea of pediatric AIDS, see the oral history in this series with Arthur J. Ammann.

[2] Corea, The Invisible Epidemic, passim.

diagnose], which is a slow-moving disease that takes so much time [to manifest]. If there were appropriate resources available for this epidemic, then we would have never gotten into this discussion. We knew women were at risk [for AIDS]. We knew women were at risk because of intravenous drug using; we knew women were at risk from sexual contact with an IDU [intravenous drug user], and that the chain of transmission was male IDU, or female IDU, to baby, and baby gets infected. That was known in 1982.

If the government had put in resources, and CDC had delivered prevention programs, they would have targeted these folks. The problem was, there was no commitment, no money. So what you had was a bone with a little bit of meat on it, and the health care hyenas were trying to take care of these people who were dying on the street, [and] the prevention hyenas were trying to snatch their piece. All CDC had was about enough money to pay for surveillance. They didn't need any more cases, because if they broadened the case definition, there weren't enough people to even interview the cases and get the forms filled out.

So the issue was a resource issue, and it got CDC caught in a lose-lose situation. Why did I ask to leave Atlanta? I asked to leave Atlanta because I felt I was on a losing team. It wasn't that the team there was bad; there were some good people in Atlanta. But the resources and government above it were going to ensure that team would eat it, and CDC was going to get criticized. I don't like being on a losing team, so I came to California. In many ways, we were all going to lose on AIDS, because of the ten-year incubation period. Even in the best society, we were going to eat it, because societies have not learned to deal with a ten-year incubation period phenomenon at all. We have not yet reached that kind of social advancement.

Hughes: Because we don't look that far ahead?

Francis: Because we can't look that far ahead. Generally, government reacts to today's crisis. AIDS is not a disease you get into if you want to win. You're going to get criticized and screamed at and yelled at, because the system is destined to political failure, and you're part of the system.

But I think many of these individual issues are peripheral to a leaderless, resource-lacking federal effort. Because of its weakness, the federal government was going to get criticized--deservedly. It was going to be one issue that was clear, and everyone was going to say, "The goddamn government, we've got to beat the shit out of it because it did a bad job." And if you're sitting in Atlanta, you're going to get the shit beat out of you.

AIDS Testing

Hughes: You said--I'm paraphrasing--that the definition of AIDS should be HIV infection.

Francis: Sure.

Hughes: But there were political pressures to make it otherwise. Would you explain?

Francis: The outspoken gay community to this day resists testing. California has been much better than the rest of the country, especially New York. New York essentially made it impossible to get tested, because you couldn't test unless you went to a government facility. I believe this test should be given to every American at risk in high prevalence areas. When they come to their doctor, when they come to a jail clinic, when they come to a drug treatment clinic, everyone should be getting this test on a routine, voluntary basis.

Because of people like Bill Dannemeyer and Jesse Helms and Ronald Reagan scaring people with the threat of quarantine, isolation, not to mention stigmatism and loss of health insurance, that recommendation has not been feasible politically. I think it's horrible. Last year I wrote an editorial that the case definition should be HIV infection, and we should care for everyone.[1] We should as a government open our arms to say, "Come, if you're HIV infected, we'll take care of you completely. We'll give you a job; we'll give you transportation; we'll give you housing; we'll give you drugs; we'll give you everything. Anything you want."

Because infected people are potentially dangerous in a public health perspective. We shouldn't quarantine them; that's too expensive and it's not needed. But we should have an isolation around them that is a voluntary isolation that we can instill in them through ongoing education and support. Then we teach everyone else to be damn careful, saying, "You have to assume everyone else is infected." But burying your head in the sand and not wanting to take on these expenses is crazy. We should welcome these folks, and we don't.

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[1] Toward a comprehensive HIV prevention program for the CDC and the nation. Journal of the American Medical Association, September 19, 1992, v. 268, 11:1444-1447.

Isolating and Sequencing the Virus

Hughes: You've spoken of CDC and the Pasteur and Gallo regarding isolation of the virus. What about Giovanni Battista Rossi and his colleagues who in September 1984 isolated the virus?[1]

Francis: I know nothing about Rossi's work. The other one is Jay Levy. Jay Levy got the virus from the French and then made isolates himself. Then he did the same thing that Gallo did, and changed the name, and did not compare his isolates to the French isolate. I think he presumed that they were the same. That's kind of the NCI approach. He didn't release the results in a press conference like Bob did, but you can make the same criticism: Why did he call it ARV [AIDS-associated retrovirus]? When we isolated the virus at CDC, we compared it to LAV and found it to be the same. We then called it LAV. That was the only proper way to do it, if you're ethical.

But yes, Jay was early in on it, no doubt. I don't know the history of Jay's lab, how long he was working on it, but he got the virus from Jean-Claude. He was over at Pasteur and picked it up, and said, "Let's see if we can do the same thing you did." Which is perfectly acceptable. And he gave references to the French in his publication, not like Gallo. He didn't go around saying, "You've got to change the name of the virus," and all that crap.

Hughes: What about Abraham Karpas at Cambridge who in December 1983 published an electron micrograph of a virus found in the blood of a gay man?[2]

Francis: I don't know exactly what Dr. Karpas was doing.

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Hughes: What about Paul Feorino?

Francis: Yes, he was at CDC.

Hughes: What did he do?

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[1] Mirko Grmek, History of AIDS: Emergence and Origin of a Modern Pandemic. Princeton, NJ: Princeton University Press, 1990, p.74.

[2] Grmek, History of AIDS, p.68.

Francis: He worked for me in the lab. It was the Feorino paper which compared the American isolates to the French.[1]

Hughes: Let's talk about the sequencing of the virus.

Francis: Well, that was really very interesting. I had never thought that HTLV-IIIB would be the very same isolate as LAV. I knew the French had sent it to Gallo, and he used their techniques to grow it, like we did. But we had LAV growing in our lab, and ultimately IIIB growing in our lab, and we had our own various isolates growing in our lab. With such numbers of isolates you always have a risk of contamination; there's no doubt about that. That's not new in virology.

Ci Cabradilla from CDC actually came to Genentech. I sent him out here with virus to do sequencing, and one of the first sequences came from that effort. Actually, my first understanding of this really came from Simon Wain-Hobson from Pasteur, who came to CDC to visit and said, "Look at these sequences, Don." He actually was even far cleverer than that. Not only is there a dominant sequence, but there is a defective subtype in LAV that varies in its percentage makeup of the total nucleic acid in the virus preparation.

Hughes: Which makes it very characteristic. Is that what you're saying?

Francis: In the LAV cultures from Pasteur, [the sequence] changed over time. So if you take a virus and sequence it, he can tell you exactly when that virus sample was sent. So he knew that IIIB was LAV and he knew exactly when that was sent from Pasteur to NCI. That put a different aura on the problem, and made it even more outlandish.

But frankly, unless someone tells me the Gallo lab took LAV, purposefully put it into a pool with other material, and decided to call that IIIB--until I hear that, I will always give the benefit of the doubt that it was a contamination in the laboratory. Now, those who have done the investigation and seen the lab books will probably have a different opinion than I have, because it looks like Gallo was growing LAV in the laboratory and put it into the pool and claimed he discovered a new virus. That's probably what happened. And when that comes out as truth and I get those facts, then I may change my opinion and possibly be very critical. But until that point, I will give the benefit

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[1] P. M. Feorino, V. S. Kalyanaraman, et al. Lymphadenopathy associated retrovirus infection of a blood donor-recipient pair with acquired immunodeficiency syndrome. Science 1984, 225:753-757.

of the doubt and assume it was a laboratory contaminant. It's happened in other laboratories. That may be sloppy lab work, but it can happen to all of us.

Hughes: And it had happened to Gallo.

Francis: And had happened to Gallo, and could have happened to me. The fact that it was a laboratory contaminant makes it even more sleazy, but it's not a great revelation. We had more viruses from Americans growing at CDC than they had at NCI. All this forty, fifty, sixty isolates may be a bunch of bunk. That's my understanding from those who have seen the lab books. That puts another horrible twist on the whole episode.

If then, as John Crewdson and others say,[1] you can trace LAV through MOV [another name given to the same virus isolate] into the pool, and everyone in the Gallo lab knew that. That adds another level of culpability and dishonesty to his laboratory's behavior. I think the truth will come out with time. The trouble is, the tincture of time tends to say, well, Bob does things like that. The same thing I was telling you about when he asked me to leave the room. instead of shouting and yelling and saying, "You jerk, I'm not going to leave the room. We're from the same institution,"--or the same department in different agencies. Instead I said nothing. People will accept Bob and it will just go on and on and on. And no one wants to deal with the old history. It's a waste of time.

The NIH-CDC Relationship

Hughes: Let's talk about the relationship between NIH and CDC. NIH is perceived as the bastion of basic science; CDC is perceived as doing applied science. Yet you yourself were doing some basic science.

Francis: Yes, but our basic science is applicatory in nature. CDC has discovered lots of bugs, and that's their job, looking for bugs. Legionnaire's, et cetera, et cetera. That is part of CDC's role, and indeed does overlap with NIH to an extent in those areas. CDC by and large is better suited to search for new causation. My wife's work on Reye's syndrome: People had been working on Reye's syndrome for years, including CDC in the laboratory. And

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[1] John Crewdson. The great AIDS quest. Chicago Tribune, section 5, November 19, 1989.

epidemiology often breaks those nuts well before the laboratory does. I think there are many, many examples of where CDC has uncovered tremendous findings in infectious and noninfectious diseases.

By and large, the basic science of NIH and the applicatory science of CDC are really quite separate, but there is a layer of overlap. That layer of overlap I think is great. One, we share a lot of resources. During my work at CDC, I had always dealt with the National Institute of Allergy and Infectious Disease [NIAID]. We were competitors, but only in that little bit where we overlapped. They were doing their thing and we were doing our thing, and that allowed us one, to have a connection; and two, some competition in government agencies is good, because it keeps everyone working just a little bit harder.

Dr. Xu Zhi-Yi and Liu Chung-Bo and I did a remarkable study in China addressing the question if you could interrupt perinatal transmission, mother-to-infant transmission, of hepatitis B virus with vaccine. HBV [hepatitis B virus] transmission from mother to infant was the major leak in our vaccine strategy for the developing world. An awful lot of these kids end up getting cancer of the liver and chronic hepatitis. China was the one place that didn't want to use any immunoglobulin because of the expense. Thus, we could just use vaccine alone to see if it worked. In places like the United States, immunoglobulin was considered the standard of care.

So we did a vaccine study of infected mothers in China. Now, what vaccine did we use? We used NIH's vaccine. Bob Purcel, from NIAID, and I would go to China. He supplied the vaccine; I would do the epidemiology. Some of our work was competitive, but it was very close and we would collaborate. So I think that was very healthy.

The relationship with NIH changed with NCI, because they didn't collaborate well, even within NCI. They seemed to hate each other. They are set up on the academic, kill 'em, fight 'em mode of operation, not on the collaborative mode. They would set out these channels of Bob Gallo's fiefdom, and Stu Aronson's fiefdom, and George Todare's fiefdom, and all these fiefdoms, all of which were fighting each other. Before 1982, I didn't ever have to deal with NCI. It wasn't until AIDS came along that our infectious agent, unfortunately, was in NCI and Bob Gallo's area. It was a totally different working relationship compared to NIAID.

Now, I knew Bob Gallo from Max Essex's lab and considered him a friend. I was part of the club, recognized. I came from

Max's lab and was on the inside, and Bob would call me and say, "Don, you only work with us. Don't work with the French. Don't work with other people." I said, "Bob, I recognize that I am a member of the club, but I'm also an employee of the Centers for Disease Control and I can't define research alliances like that. I've got to work in a general public health sphere, and if people want specimens, I send them, if they can handle it and they're reasonable researchers."

But in general, our relationship with NIH I think is good. At least with NIAID I've always enjoyed it. I've kind of enjoyed the competition.

Hughes: Shilts quotes Gallo as saying that the research that was being done on the retrovirus at CDC was a "duplication of government expenditures."[1]

Francis: Right. You had this huge epidemic, and he's saying you don't need two laboratories to work on it. That's relatively self-serving. [laughter] He was saying the CDC does not need a laboratory to work on AIDS. It's just nonsense. He also made it very clear that he wanted to close down our lab.

Hughes: Were you privy to what was going on between NCI and NIAID?

Francis: Yes. Bob called me and said, "I don't want to announce this virus until we have full control over it, because I know it will go over to NIAID." He saw the writing on the wall. And it did. He still maintains a great deal of control, but NIH recognized that there were other people who had worked with horizontally transmitted agents that were far more talented than Bob Gallo's group was.

AIDS Units at CDC

Hughes: There were several branches of CDC that were engaged in AIDS-related activities. For the record, the Center for Preventive Services, the Center for Health Promotion Education, Training and Laboratory Program--which was you, right?

Francis: No, that was a separate group. I was the Center for Infectious Disease.

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[1] Shilts, And the Band Played On, p.366.

Hughes: That's the fourth one. How coordinated were these activities?

Francis: Initially, it was a very small group of people, and relatively easy to coordinate. Hard to do, because no one had the full time to do it. CID, the Center for Infectious Disease, was always the headquarters of the knowledge base, and we would bring in other groups. By the time I left for California [1985], I within CID had designed the first national prevention program, not from the Center for Prevention Services [CPS]. But Prevention Services was traditionally the one that delivers prevention programs. With time, I moved over to Prevention Services in my California assignment.

By that time, as the national budget started increasing, the coordination became terrible. And to this day, there's not the best relationship between CID and CPS. An attempt was made to change that by putting somebody in the director's office at CDC in charge of AIDS. That was initially Gary Noble, and now Jim Curran. That just adds another layer of bureaucracy. There's no center for AIDS, and that's what has to be done. You have to make a center, and all these folks are in that center, and the work goes out from them. We've made that recommendation through an expert committee advising CDC. Whether it will ever happen or not, I don't know. [Added by Dr. Francis during the editing process: It has.]

Hughes: Was it a CDC committee looking at CDC?

Francis: No, it was outside CDC. I was retired from CDC by that time. It was a CDC-arranged committee, but with outside-CDC advisors.

Hughes: When was this?

Francis: Just last year [1992].

Hughes: How big a role did the Center for Health Promotion and Education play?

Francis: Early on, it had very few people, so it was just kind of advising. These were the experts in health promotion; they had to come over to us, single-shot folks, and try to give us some advice. And they were always involved in advising us. However, with time this negative division began to emerge: the epidemiologists on one side and the behavioral change experts on the other. To function effectively, the expertise for the epidemiology has to sit with or close to the prevention folks. You can't have them separate, which is what was done. The result has been the prevention folks with the techniques for behavioral change without the expertise in epidemiology. So it has been a

terrible setup, because most of the scientific expertise resided outside of the deliverers of prevention programs. With time, the prevention program deliverers became contract-writers without any expertise.

What CDC does is imitated by the expertise and desires of states, and what the states do is imitated by local governments. So what we have ended up with is these contracting-type people running prevention programs who don't know anything about either the epidemiology or the behavior change modalities. Hence the CDC model has been a sadly replicated one at state and local levels.

Hughes: How does the AIDS Activities Office fit in?

Francis: This was the centralized group that was supposed to coordinate all of this work on AIDS.

Hughes: And does?

Francis: Oh, it tries. That is another group at the federal level trying their best but working without true authority. Line authority is important to get things to work. To this date, it hasn't existed. It's been matrix managed outside of a line authority, which is a total disaster.

Hughes: Would you talk about division of labor between Jim Curran and you?

Francis: Well, our responsibilities were fairly clear. This was all in CID in the Division of Viral Diseases, of which I was the assistant director. And then we had the AIDS Activities Office, Jim's office, in CID. I took over directing a laboratory to complement and work with Jim's group. As I told you, Jim asked me to do that from Phoenix. That was something that goes back to 1981. And I said, "No, I don't want to; I'm doing all my hepatitis stuff. I'll help from the sidelines. I'll be on the [AIDS] task force; I'll [help] by telephone, but I can't coordinate the lab in Atlanta from Phoenix."

But, as I told you, the pressure just mounted and mounted and mounted, and there was just no way to manage the effort. Every time I'd go to Atlanta to get stuff organized, I'd turn my back and it would all stop; everyone would go back and do their own research, and AIDS would never get the appropriate attention. At that time, everyone was defending their turf, because budgets were being cut, cut, cut, cut. People, supplies, and equipment. In that setting, the worst thing you can do is volunteer some of

your staff to help out on another job, because you know you're going to lose them [permanently].

Luckily, I was assistant director of hepatitis, so it was easy for me to volunteer my time. But hepatitis lost me. I don't think they ever got my position back. Jim was lost from the Sexually Transmitted Diseases Division. STD deserves a lot of the credit for the heroics here, where they gave all these people--Bill Darrow, Harold Jaffe--at a really tough time. The director of STDs, who was Paul Weisner, said, "This [AIDS] epidemic is important, we've got to work on it. It's our [CDC's] responsibility." And he really ate it. I don't know if STD ever got those positions back.

General Accounting Office Audit of CDC AIDS Activities, 1983

Hughes: In 1983, the General Accounting Office [GAO] audited CDC's AIDS surveillance program, AIDS lab studies, and AIDS epidemiology.[1] Senator Ted Weiss on a subcommittee of the Committee on Government Operations asked for an audit. Does that ring bells?

Francis: Yes, Mr. Weiss and Bill Foege [CDC director] got into a pissing contest over it. Being from New York, Ted wanted to find out what CDC was doing about AIDS. We in AIDS work at CDC were letting it be known that we were not able to get done what needed to be done.

Hughes: Why was that inquiry appropriate from New York?

Francis: Because of all the AIDS incidence in New York. Mr. Weiss sent a woman down--I forgot her name--very good, but she wanted to see our files. Our files are full of patients' names. And in public health, it's really sacrosanct that you don't let people from the outside, especially from any other branch of government, or for that matter anyone else, come in and pull people's names out of files.

She wasn't going to reveal anyone's names, and she knew it. But we couldn't know that. She and Bill Foege got in a tremendous confrontation. It progressed to: "You cannot come into our offices." Instead of, "Come on, let's work together, and figure--." Bill is a very collaborative person. But

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[1] Sandra Panem, The AIDS Bureaucracy. Cambridge, MA: Harvard University Press, 1988, pp.31-35.

something happened, and so it got to be this huge thing and she assumed CDC had something to hide. Well, we didn't have anything. What was hidden was that we were doing a crappy job, because the administration was not giving us the resources we needed. We needed that message to get out. The whole thing wasn't played well.

CDC had this naivete, and I had it until I came out to California: We're doing good things; we're expected not to have any resources; we eradicated smallpox on a shoestring; we can do anything. Really, the opposite of NIH and NCI saying, "We need to get into politics and raise money," because money was at least a necessity to get your job done well. So we didn't play the politics very well.

I don't know why Bill hit head on with Ted Weiss. It should have been a collaborative effort, because both CDC and Ted Weiss wanted CDC to do a better job. Instead it got into a really horrendous privacy conflict. They thought we were hiding something. So I guess a GAO [General Accounting Office] audit was asked for. I think it concluded that CDC just couldn't do what we asked it to do with the resources it had. In the end it all came out fine, but it was not pleasant.

I remember bits of it, at least. I saw the investigation as an invasion of my work. I had my fifteen-hour day; I didn't need to take an extra hour for some congressional person to talk to me. What I didn't realize is that they were the key to saving me from this impossible, resource-strained situation. We were in our politically isolated little place; we wanted to stay there. It was really stupid.

Hughes: Eventually, the CDC released some of the information without reference to patient names.

Francis: Yes. It meant that staff had to go through the files and take off every name. If someone came and told me to do that, I'd just tell them to get out of my office. I didn't have the time to deal with that.

Hughes: But somebody apparently did it.

Francis: Yes. It's very expensive.

Hughes: Did some good come out of that episode?

Francis: Oh sure. Ultimately it was Ted Weiss' committee before which I testified about CDC's shortcomings. And Ted Weiss was terrific. He died soon thereafter.

Hughes: Your testimony against CDC was more or less the same as what you said in the 1992 JAMA article?[1]

Francis: Except the new director of CDC (William Roper), when I testified was out of the room. I was in the leadoff group. Bud Roper, from Roper Polls, was the first. He said, "The American public sees AIDS as a problem, and has personalized it already. They see it as a risk to them and their children, and they want frank messages out there to tell us what to do." I came up and said, "CDC has been prevented from doing its traditional job in public health by right-wing politics."

Then Bill Roper, director of CDC, no relation to Bud Roper, comes back into the room, having not heard our testimony, and says, "Well, the reason that we don't have any mention of condoms in any of our national AIDS education programs is because the American public really hasn't personalized the risk of AIDS. The first thing we want them to do is to feel the risk of AIDS, and then we'll come up with the necessary information, but we don't feel the American public has personalized it yet." He hadn't listened to Bud Roper.

Then Ted Weiss asked him if he had had any political interference, and he said, "No, I don't have any political interference at all." Just after I, who had been at CDC ten times as long as he had, said I'd never seen such political interference in my whole career at CDC. Ultimately that ended Bill Roper's job. I don't even think he knew what happened. Just because he was too busy, wanted to make some telephone calls, and wouldn't sit and listen to testimony that preceded his.

I learned very early after coming to California that when you're testifying in front of a committee, you better sit through that whole damn testimony and hear everyone's testimony. First, because what you say, especially your written testimony, can become meaningless or redundant. Second, you better hear what somebody else says against you.

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[1] Donald P. Francis. Toward a comprehensive HIV prevention program for the CDC and the nation. Journal of the American Medical Association 1992, 268, 11:1444-1447.

Communicating on AIDS

Expedited Publication

[Interview 3: February 11, 1994] ##

Hughes: Dr. Francis, I read that Edward Brandt early on in the epidemic--I don't know the year--requested that leading medical and scientific journals expedite publication of AIDS papers.[1] Did the major journals actually do that?

Francis: This really centered around a rather bizarre policy that the New England Journal set--other journals tended to follow, and certainly scientists followed--that you couldn't talk about your results anywhere if you expected to get them published later in the New England Journal. That is, if they were announced publicly, New England Journal wouldn't publish the research. This was really a repressive policy--stifling scientific communication. Publication takes months and months. Public discussion in meetings and other gatherings is the best way to announce the latest findings and get information out. So this policy slowed scientific information exchange by several months. It was terrible. It was primarily New England Journal. I don't know if any other journals officially followed the NEJM, but researchers felt that they did, or might, and so they were very reluctant to make these announcements [before publishing].

For the good of the public's health, we had to let AIDS information out ASAP, and yet people who did the research were reluctant to allow it because it would take the wind out of the publication sails, and make it less likely that they get their research published. It was a silly little problem, but one that I think the Assistant Secretary of Health and Human Services did make an active decision to do something about. I don't remember exactly when he did that.

Hughes: How did you get critical information out?

Francis: Well, the MMWR is the way CDC gets it out primarily, and then scientific meetings. The annual international conferences on AIDS started in 1985, and there were always multiple conferences even before that and in between, enough to drive you nuts. But we would try to present the latest data that we had whenever we'd speak.

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[1] Sandra Panem, The AIDS Bureaucracy, p.111.

Hughes: So you didn't feel that there was a problem in disseminating information?

Francis: Some people did; the blood banks complained that they didn't have all the information, but indeed they did if they just listened.

Censorship

Hughes: Were you given free rein as a member of the CDC to say anything that you wished to the press or to whomever? Was there any censorship?

Francis: Early on, it was typical CDC where the press was sent down to the person doing the investigation, and there was essentially no control. Later, once Reagan came in [1980], we were almost totally censored. Some of that was political from Reagan's side; some of it, though, was our setup that we actually prescribed because when something about AIDS would occur, you'd spend the whole next day responding to the press, and it would eat up all your time. So we said, as I mentioned earlier, "Well, let's let the press office deal with this stuff instead of us," because we were so understaffed. That was a mistake, because it set up a situation which the scientists didn't control. By the mid-1980s there was no unapproved discussion with the press, and Washington could come down very heavy on you if you did.

Hughes: What sorts of things were censored?

Francis: Any claim for additional resources. That's what they wanted to control. They didn't want the scientists out there saying, "Well, we just don't have that information because we don't have the resources to do this job." And it was not just for AIDS; it was for everything. The administration did not want government employees saying they can't do a job because they don't have enough resources. If they did, they wouldn't be able to cut budgets.

Dealing with the Media

Hughes: Was there ever a problem of translation when the press office at the CDC handled matters?

Francis: Yes and no. They were very able people who understood at least the general aspects of a story. Some press people really know what's going on, and those subtleties that the press really would like were missed.

Hughes: Were there particular people in the media that you dealt with?

Francis: Yes. Larry Altman of the New York Times was clearly a person that I talked to, and he would drop by CDC periodically.

Hughes: Why did you choose him--or did he choose you?

Francis: Larry Altman is a doctor who was at CDC during his training, so he knows epidemics and epidemiology very well. Who else? There was Chris--forgotten her last name--of the Washington Post. There was Marlene Cimons of the L.A. Times. And of course, Randy Shilts and others from the San Francisco Chronicle. And then there was an obsessed guy named Chuck Ortleb from the New York Native who was always on my telephone driving me nuts about African swine fever virus. He lost it--like Peter Duesberg at Berkeley. These people get this pit bull approach to science and lose all ability to look at data.

Defining AIDS

Broadening the Definition

Hughes: We talked last time about defining AIDS. What were the forces changing that definition as time went on? Was it just science?

Francis: For the first years, it was all science. The definition enlarged to include more opportunistic infections and some new cancers, as we got more information. A doctor could call and say, "Lookit, this guy doesn't have Pneumocystis; he doesn't have Kaposi's sarcoma, but he's got cryptococcal meningitis and he's a gay man with no T cells. He clearly has your disease [AIDS], but he doesn't meet the definition." And so we said, "Gee, that's really a rare situation." So with a little review of the literature, we said, "Okay, that individual fits into the AIDS definition."

Hughes: What would reviewing the literature accomplish?

Francis: It allowed us to estimate what the incidence of that opportunistic infection was in other immunologically normal

individuals. And so the list of opportunistic infections that fit increased with time. The technology to identify and diagnose some of these organisms, cryptosporidium especially, improved with time, as did Pneumocystis, and so some criteria changed.

And then came another scientific issue, especially with Kaposi's sarcoma: Doctors weren't necessarily doing biopsies of these tumors. Initially CDC required a biopsy diagnosis. Similarly, with Pneumocystis, the doctors got so familiar with it that there was no reason to spend the extra money or pain to do a biopsy or bronchoscopy. They could just say, "That's Pneumocystis," and "that's Kaposi's sarcoma," and treat them. So there were these provisional AIDS diagnoses that later became acceptable.

Only in the last few years was there the political issue. It's fascinating: Early on nobody wanted to have an AIDS diagnosis; they didn't want to be in a risk group. But once they realized that resources tend to be allocated to those groups with higher incidence, the desires changed. This was highlighted with women who had different clinical syndromes such as chronic yeast infections and the like. That pushed the whole issue of diagnosis of "AIDS" into being 200 helper cells [or less]. But by that time [after March 1985], the HIV test was available, and frankly, the diagnosis at that point should have been HIV infection. But AIDS activists still resisted reporting HIV infection, as they initially had for AIDS.

Hughes: Why?

Francis: Oh, I would say it's an old, old thing that if people are healthy, you don't want their names in some government computer. It makes no sense whatsoever. But there's sensitivity to HIV reporting to this day; people don't want to be reported, period. They do once they get AIDS and there is benefit from the diagnosis because of resources that may come forth. But short of that, they don't want their name in somebody's computer. Yet to my knowledge, essentially nobody's name has ever leaked out of the government computer, and there's, what, over 300,000 people with AIDS in these computers now. Privacy has been well protected, as it has been traditionally in public health. But there still is a sensitivity.

The issue of wanting an AIDS diagnosis to be broadened was also complicated by the fact that the Social Security Administration made the clinical diagnosis of AIDS part of their eligibility criteria for their Social Security benefits. CDC made epidemiologic definitions that had nothing necessarily to do with disability. For example, people with Kaposi's sarcoma can

be quite healthy early on; they just have a purple spot somewhere, but other than that, they can work for years and do fine. But KS patients were considered disabled because they had an AIDS diagnosis, whereas somebody who had a wasting syndrome didn't meet the case definition in the early days, but was sicker than a dog, and couldn't get out of bed in the morning. But that person was not "disabled." [tape interruption]

Defining AIDS as HIV Infection

Francis: But the real issue now is HIV infection. I've written an editorial suggesting that we report HIV infection, and deal with the disability issue separately, and don't connect the two.

Hughes: Why, after it was possible to determine HIV infection, were opportunistic infections retained in the definition? Why not just have HIV infection?

Francis: HIV infection is reported in many states, but in the big states, the gay community has lobbied against it because they were worried about privacy violations and other rights violations. In California, after all, Bill Dannemeyer and his incredible group tried to pass a quarantine proposition on the California ballot. You can see how they might be afraid. Perception can be very important.

Hughes: So that's where the politics comes in, rather than the science.

Francis: Yes.

Hughes: The definition would be just HIV infection, if it were based strictly on science?

Francis: Yes, absolutely.

Hughes: What are the ramifications of the fact that it is a more complicated definition?

Francis: Let's look at the reasons for reporting: one is to get preventive services, two is to count new infections and get some evaluation of the effectiveness of your prevention program, and three is to make long-term planning for caring for these individuals. And you want to get all that information as soon as possible after the test has been discovered. Any delay hurts all those parts of your program.

Including Women's Symptoms

Hughes: There has been criticism of the fact that the official case definition, until 1993, did not include symptoms that were specific to women. Is there any justification for that criticism?

Francis: Some. Women's chronic yeast infections and the like can occur without AIDS, and so it needed to be a definition that would be linked to HIV infection. A simple solution may be to say women meet the criteria if they're HIV positive with T cells below 200. But again, if you really want to track the epidemic, you would request reporting of HIV infections. If you want to evaluate the trends compared to the old definition, then keep a subgroup where you continue to use the old definition and say, "Ah, now they've reached that definition, I will report them for comparison reasons and see what the epidemic is doing in relation to what we did in the past." The continuing debate about definition outside of HIV infection is all kind of nonsensical, in my opinion.

Hughes: Is it common for an official definition of a disease to change over time?

Francis: Certainly as the technology improves, yes.

Hughes: Well then, how do you ever get an accurate longitudinal study?

Francis: Makes it hard, there's no doubt. If you want to keep an accurate longitudinal count, you'd have to at least keep a portion which was collected in an identical manner as previously.

But with HIV, it's not a great problem, because we know the natural history well enough where on a computer you can say, "Okay, we know that if we shift the definition to a new one, we can predict the effect accurately." We know what the natural history is.

Hughes: It's a problem to some, however, who maintain that the new definition magnifies the number of AIDS cases.[1]

Francis: Nobody's magnifying anything. You change the definition, we can calculate exactly what that means. Those are critics looking for some simple hit.

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[1] See, for example: S. W. Chang, M. H. Katz, S. R. Hernandez. The new AIDS case definition: Implications for San Francisco. Journal of the American Medical Association 1992, 267:#2:973-975.

Hughes: Activist groups drive this politicization of the definition? Is it as simple as that?

Francis: Yes. But they don't want to push it all the way to HIV reporting. [laughter] Isn't that interesting?

Hughes: Yes, it really is.

Coining the Term AIDS

Hughes: Were you at the CDC meeting in July 1982, where the term AIDS was first coined?

Francis: Yes, I was.

Hughes: Can you tell me about that?

Francis: It was at the hemophilia meeting in Washington, D.C., and Bruce Voeller, who was I think chairman of the National Gay Task Force, recommended that we approve that name.

Hughes: Had he thought it up?

Francis: It actually went out in the invitation to the meeting. Dr. Foege from CDC used the name "acquired immune deficiency syndrome." So it looks as though it came from CDC. Then Bruce is the one that said, "This is what it should be," and everyone voted on it and that was it.

Hughes: Did the term strike you when you received the announcement?

Francis: No.

Hughes: Because it fit your perception of the disease?

Francis: Sure.

Hughes: Was there any reaction from anybody else?

Francis: No, that was not a big deal.

Hughes: The reason I ask is because some of the previous names had been a big deal, for example, GRID [gay-related immune deficiency].

Francis: We never used GRID. That was, I think, a local New York term. Since we already had IV drug users, why would you call it GRID?

Hughes: What were you calling it before that meeting?

Francis: KSOI [Kaposi's sarcoma/opportunistic infections]. Rather clumsy but descriptive.

The HIV Antibody Test

Screening Blood Samples, 1984

Hughes: Please tell me about your use of the HIV antibody test.

Francis: When we, with the collaboration of Institut Pasteur, got our test cooking in about February of '84, I immediately went down to our freezers and pulled out samples, primarily from the gay community in our different study cities, to see what infection rates existed at different times. We started studying samples straight away. It was just a matter of how many your lab could test if it was running full steam, all day long.

Hughes: Were other people doing the same thing?

Francis: Yes. But the test existed only in a few laboratories at that point.

Hughes: Levy, I know, had one.

Francis: Jay Levy got his going a little later, I guess. Bob Gallo had his; Institut Pasteur. We all had relatively crude tests. But they were very good, very predictive for high-risk populations, where one false positive doesn't make any difference. But in low-risk populations, it was a problem, because the cutoff would pick up people who were not really infected.

Hughes: Did you learn anything that surprised you?

Francis: Oh, yes. The extent of infection surprised us. We're talking about 50, 75 percent of our samples from San Francisco being positive, and 20, 30 percent from St. Louis, Denver, and Chicago. Then the natural history data started to just be horrific. The major thing that came out was that, of the people infected, almost all had had abnormal T cells, and a lot of them had already died, about 6 percent, I think, on our first cut. Now, 6 percent mortality for a viral infection is incredibly high.

Hughes: How did such statistics compare to your experience with other infectious diseases?

Francis: I come from a very biased experience: Ebola, smallpox, Lassa had extremely high mortality per infection, where something like polio, less than one in 1,000 people died. HIV was already at 6 percent mortality; that put it up there in the viruses that we kept in the hot lab at CDC, the really dangerous ones. And then when we started estimating using appropriate statistics, it was clear that the percentage was much higher than 6 percent. So that was really incredibly impressive and worrisome.

The Issue of Safety

Hughes: What were you thinking about your own personal safety?

Francis: We were all very concerned.

Hughes: More so after you had the results of antibody testing?

Francis: No. I had very strict rules in the laboratory, because I recognized that historically the first people that come down with a disease after the original cases are the laboratory workers, and I didn't want anyone in my lab dying of this disease. So we were very strict. But as soon as the test became available in our lab, I immediately required, asked, everyone to be tested. There was a hue and cry at CDC, interestingly, saying, "Well, you really can't do that, because somebody might be gay and test positive." I already knew who was gay in my lab. CDC said, "Oh, we've got to bring this through the ethics committee," and all this stuff.

I just sat down with my lab folks and I said, "Lookit, I think this is just ridiculous. We need to know whether we're protected here or not. We have spouses, and we want to know whether the precautions we're taking are adequate," because we were up to our elbows in that virus for years. So they all agreed that we be tested. The CDC told me not to, and I went ahead and did it. I threw in a couple of positive specimens we had from chimpanzees so that the laboratory technicians wouldn't know if someone tested positive. I was the only one that had the code. We tested everybody, and luckily everyone was negative.

Testing Advocate

Hughes: I understand that you took quite a firm position on the necessity of widespread testing.[1] Why?

Francis: We had relatively few tools to deal with this virus in a public health sense. When you have a disease that's relatively difficult to transmit, not like influenza that spreads like crazy, but rather one that goes from person to person to person, the chain of transmission becomes terribly important. Finding an individual who's infected, so that he/she can be advised, along with their sexual partners, on how to protect themselves, is incredibly important. In the end you are dealing with the ends of the chains of transmission where an infected person is having contact with an uninfected one. In order to do that, you have to know who's infected and who's not. That's where the test comes in.

So I've been a very strong proponent of widespread testing, including in areas like California where I think essentially everybody in a given age group should be tested so that all HIV infected people know they're infected, so they can learn how not to transmit it to others.

Hughes: What has been the reaction to that viewpoint?

Francis: I think in California, we haven't followed through with it. The California Medical Association was in support of it, and some of the gay groups were in support of it, as long as it was voluntary testing and not mandatory. What is essential is a place where these people can go after they are identified as being infected. We must have some medical system that can handle and take care of them. We called it "early intervention." I think most people are in favor of it. The trouble is, the latter part (the medical, counseling, support system) doesn't always exist; there's not enough money to take care of all these people, so the program of widespread testing is only passively accepted.

Hughes: I read about a workshop on HIV antibody testing that occurred in July 1985, sponsored by the FDA, CDC, and NIH.[2] Does that ring any bells?

Francis: Yes, I remember that, but I don't think I went to it.

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[1] Shilts, And the Band Played On, p.469.

[2] Sandra Panem, The AIDS Bureaucracy, p.115.

Hughes: The various manufacturers of the test made presentations in the afternoon, and they were not forthcoming on the scientific details, for trade secret reasons.

Contact Tracing and Partner Notification

Hughes: Contact tracing and notification go along with antibody testing?

Francis: Yes, contact tracing is clearly part and parcel of the whole program. That was strongly resisted by the gay community. I remember Marc Conant and me meeting with the National Gay Task Force--at least with Jeff Levi and his group in San Francisco Marc and I were asked to come down and discuss partner notification, which the gay community was strongly against for years. There we have a little different issue. Wanting to be voluntarily tested is one thing, but if you as a male tell a government worker that you had sex with another man, that clearly meant that you were having homosexual sex, and the man whose name was just given did not have any informed consent about being mentioned as a sexual partner.

What was silly was that we had been doing this for years with syphilis, and indeed some gonorrhea partner notification. Much of this was with gay men, so this was not a new phenomenon at all. But yet there was this hue and cry about it, and it continues to this day. The reason being not that they wouldn't support it if it were something that was important for public health. Unfortunately it became political. The Dannemeyers and all pushed partner notification like crazy, and so the gay community felt an obligation to resist it. That got it into a terrible bind. To this day, partner notification is not terribly popular.

Now, in what we call the early intervention model, where all infected people are brought into a medical, social, behavioral longterm follow-up program, partner notification becomes an integral part of what one's responsibility as an infected person is. There's a system into which people who test positive are enrolled, and it all works out very well. But the fifteen-minute partner notification format is hard on client and clinic if you don't have a well-resourced program.

Hughes: Are you saying that if a person is going to participate in one of these programs, the understanding is that it involves partner notification?

Francis: All partner notification is voluntary. We don't torture people to get names of their contacts.

Hughes: [laughs] Yes. But there is a certain social pressure, nonetheless.

Francis: Oh, yes, an ethical pressure of, if you're getting a service, and you have contact with someone else, that exposed person should have the right to know that they've been exposed, and they should get the service, too. Yes, there's a pressure. I think it's an appropriate one.

Civil Rights versus Public Health

Hughes: There is a broader historical event that underlies these concerns, and that is the rising consciousness of civil rights, which escalated in this country with the civil rights movement in the sixties, and then of course has been adopted by other groups, including the gay and lesbian groups.

Francis: Yes. It is a new thing, and a potentially very dangerous one. Civil rights are often easy hits. It's always easy to call civil rights. I remember when the gay community was saying, "It's the civil right of a gay man to be able to donate blood," the hemophiliacs were saying, "Well, it's our civil right to be protected from death." It was nonsense--there's no civil right guaranteeing that you can donate blood, and there's a health decision that goes along with that. I think we have to be very careful about this civil rights issue versus public health. When there's such a dangerous virus circulating around, we will compromise some "civil rights" for the betterment of the community.

Now, this is a voluntarily transmitted disease by and large, of relatively low transmissibility, and so we don't lock people up. If it were airborne, we would isolate infected persons as long as they were contagious, and justifiably. Isolating people with bad infectious diseases for which there is no treatment is something you have to do. It isn't necessary for HIV, because we get the information out that there is a dangerous virus out there, and hope that people change their behavior and protect themselves. We stress individual action and responsibility. If the government takes everyone who is infectious out of circulation, then you give the exact opposite message, i.e., it is safe to practice at-risk behavior.

If you give that opposite message, you better have a good program that indeed gets all the HIV-infected people out of circulation, because otherwise you'll have a fox in the chicken coop phenomenon, and you'll be a lot worse off than if you did nothing.

Hughes: Has the CDC actually quarantined people in recent years?

Francis: Sure. People with tuberculosis are periodically locked up if they don't take their pills. And they should be. They have an airborne disease that puts others at risk for just breathing air.

Hughes: And there's not a great public stink?

Francis: Oh, yes, there's some. But isolation rules are very strict. We've got to be careful in America that we balance civil rights and public health.

Community Input

Francis: Interestingly, one of the things that is new in public health is bringing in new constituencies as part of planning programs and dispersing information. Sometimes that has been a disaster. Bringing the hemophiliacs in to discuss the hemophiliac thing hurt the hemophiliacs.

Hughes: Explain why.

Francis: Because in the July meeting of 1982, the hemophiliacs' spokesman, Charles Carmen, said, "Don't take this stuff [blood and factor VIII concentrate] away from us. We know it's risky; we're willing to take the risk." Well, that kind of took the wind out of CDC's sails, and so everyone said, "Well, yeah, factor VIII is important; we better leave it on the market." When in reality, it was a convenience; it was not survival. There were other ways to get clotting factor into people--less convenient, no doubt. In this case the "responsible" community member allowed us (CDC) to abrogate our responsibility.

We also brought the gay community into many discussions. We had very serious discussions about the dangers of gay sex--especially in bathhouse-type environments. Here government was making recommendations about homosexual relations.

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Francis: Sometimes there was reluctance to take action because some would say, "Oh, you can't say that to gay men." Well, you may not say it in public, but you get leaders on the side and say, "Bullshit, this is dangerous. You must recommend change. We have to do it to save the gay community." The preventive issue is who is getting most of the infections in the United States right now; it's gay men. So they ought to be screaming for prevention and vaccines. And yet the ones who are making the most noise are the ones who are infected, and they're screaming for drugs. They don't want any money diverted to prevention. So we have a conflict of interest.

Well, public health should be making those decisions, informing the gay community, getting their support as much as possible. But if partner notification or HIV reporting is right, then it should be instituted.

Hughes: Well, where is the proper place for community input?

Francis: I think it's important to have it in place all the time, but what you have to do is be sure you know whose hat everyone has on in the room. If the gay activist is representing gay civil rights, fine. But if you're representing public health, you better take your words and action from your wisdom, not from complaints from someone about civil rights. You want to listen to those, because you want the cooperation of the community. But you should be very matter-of-fact, saying, "For the benefit of public health and, for example, the gay community, I am going to do this."

Hughes: Do you feel that there were instances when the CDC was hampered in its activities because of oversensitivity to activist concerns?

Francis: Yes. Once the Reagan administration undercut CDC, then CDC became a half-baked organization. That is, it couldn't stand on its laurels and say, "We did a good job on this, and therefore, we will take a cutting-edge stand--"

Hughes: Because of budget cuts?

Francis: Both budget and policy inadequacies. The Reagan administration had terrible policies.

Hughes: Why?

Francis: They didn't care about AIDS; they didn't care about AIDS prevention. Bill Dannemeyer told me: "All you want to do is teach these guys how to bugger better." And I said, "If it saves their lives, I'll teach them how to bugger better." And Reagan

said, "Not with government money you won't." And the director of CDC, Jim Mason, went along with it. For example, for an entire year, there was no decision on what government could say regarding homosexual health. So a year went by when there was no government funding going out there about safe sex for gay men.

Hughes: Which year?

Francis: '85, '86. So that was real government interference. Same thing on population-based sex surveys--it went on and on and on and on.

AIDS is a sensitive issue with the gay community, or for that matter any other community, Haitians and others. Public health is going to take some tough stands that are going to irritate people. That's the reality in public health; you can't keep everybody happy. But if public health practitioners act appropriately, the society will support this. But when they don't trust in public health inherently, it's very difficult to operate in these rough waters.

So when public health practitioners start making compromises--more political compromises in order to keep the gay community happy--you can hurt them. You want to walk in step with at-risk communities; you don't want a war. But you also want to be very forceful where necessary. It's a very fine line, and if that balance is shifted, by statements of extremist politicians in the Reagan administration, then it's very hard to walk that line.

Hughes: How were you as an individual affected in terms of your activities? From the little I know of your past, you were used to operating in a fashion, "Let's stamp it out through vaccination." Well, obviously, you didn't have a vaccine in the case of AIDS.

Francis: Stomp the virus out with something else--yes.

Hughes: So what effect did political considerations have on the way you operated?

CDC Advisor to the California Department of Health Services, 1985-1989

Francis: Well, first of all, I had to get out of a lose-lose situation in Atlanta, so I asked to be transferred to California, where at least the government was trying to do something about AIDS.

There I put myself into my Bangladesh mode: I never lost sight of my goal. I just had to shift the time frame when I could accomplish that goal. It was similar to what I did when I was in the developing world working for WHO. I had my things-to-do list in the morning, and when I first arrived, I was very frustrated because I didn't get everything done. Then I said, "Well, I just won't get frustrated any more. I'll just keep the items on the list for tomorrow, and eventually I'll get done." I found a balance between what compromise I could accept without just going crazy, and what I must get done.

Hughes: What could you do in California that you could not do at CDC?

Francis: I could say what I needed to say here, because I was a scientific advisor to the state of California beholden to nobody. The CDC was perfectly happy to have me do that. They slapped my hand a few times, but I was out there saying what should be done concerning AIDS.

Hughes: Now, they were willing to have you do that because you were one step removed from CDC?

Francis: Yes.

Hughes: Was it as simple as that?

Francis: And they knew they could never stop me.

Hughes: [laughs] That I can believe.

Francis: But yes, I could speak out here, including criticizing the Reagan administration. Now, mind you, I was a guest in the state, and even though this is my native home, I was still legally a guest, a federal employee on a state assignment, so I was quite cautious about criticizing the government of California.

Hughes: Which was a conservative government.

Francis: The administration was sometimes primitive. And so I would speak out sometimes in very subtle ways. The governor's office called me a couple of times and complained. But never did it amount to anything.

Hughes: You sound as though the situation in California was an improvement over Atlanta.

Francis: Oh, yes. Well, because in California we had a group of individuals, with Marc Conant, usually the president of the California Medical Association, Mark Madsen, who was a staffer of

the CMA, the gay leadership, the chairman of the State of California Department of Health Services Task Force on AIDS, be it Conant or Decker or whoever--there was a mass of people that could be rallied in fifteen seconds to stop any negative move by extremists. So I felt fairly confident that there was a power base behind me, and I could push the envelope a little further than I might otherwise.

Hughes: Did you have those liaisons before you came back to California?

Francis: No, they were assembled only after my arrival. Jim Chin, the state [State of California Department of Health Services] epidemiologist, as soon as I came, set me up to meet all these people, and through doing my job, I met everybody else. It was a pretty small group at that time [1985].

Then came California Propositions 102[1] and 64 and 69. There's a very good lesson for history from this example: Adversity is what drove us together. The California Nurses Association, California Medical Association, the gay community representatives, gay physicians, public health, business--when this crazy stuff began coming from Lyndon LaRouche[2] and from Dannemeyer, they became wonderful rallying points in favor of logic. One could really bring people together who might not agree on other issues.

Politicization

Hughes: How do you feel about politicization of the epidemic and of Don Francis? Were you forced to be a political animal at CDC?

Francis: In public health, you are always dealing with the public by nature, and therefore by nature you're always out in the public eye. But as physicians and scientists we try to stay above politics; we like being in Atlanta and not Washington. In

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[1] In 1988 the voters defeated Proposition 102 which would have required physicians to report to the state the names of all HIV-positive patients and those suspected to be HIV positive.

[2] In 1986, followers of LaRouche introduced a California initiative which, if passed, could have resulted in quarantining and discrimination against people with AIDS. (John Kinsella. Covering the Plague: AIDS and the American Media. New Brunswick: New Jersey: Rutgers University Press, p.267.)

retrospect, that was extremely naive. It's nice to have public health be independent from politics, but it isn't, and it wasn't in this case. I shifted all the way from a doctor and a laboratory scientist and public health person, to almost a full-time politician and policy person.

Hughes: Is that how you regard yourself?

Francis: In my last years in government, I was almost full-time policy. I was writing legislation; I was reviewing legislation; I was recommending where money went.

Hughes: That takes a very different set of skills. How did you acquire them?

Francis: By the school of hard knocks, and from some extremely good politicians in California, people like California state legislators John Vasconcellos, Burt Margolin, and Jackie Speier, their staff members, and even [California State Assembly Speaker] Willie Brown's office. These people are really good, and they ask, "How do you want to do this? How do you arrange testimony?" Later I ended up in the mayor's office in San Francisco [as the mayor's Special Consultant on AIDS, 1988-1992], and worked with people like [Mayor] Art Agnos who are dynamite at moving those kinds of politics. San Francisco, with its all-inclusive politics, is a tough place to work. If you can survive in San Francisco, you can survive anywhere.

Hughes: Were you conscious of watching politicians to learn how to operate?

Francis: Yes. I always watched to learn, but I always kept myself a bit above the fray. My issue was science and the public health. If I had to maneuver politics in order to favorably affect a program towards the logical scientific approach, I would do that. But I learned from my experience with the World Health Organization that if you make yourself primarily political and secondarily scientific, you'll lose your credibility and you'll be running in circles pretty soon because you'll compromise here and compromise there. So as long as you stay strictly scientific and then do the politics to accomplish that scientific endeavor, then you're always clean, even though you're in a potentially dirty situation.

Hughes: Which is precisely what you were advising the CDC to do in the speech you gave when you retired from the Public Health Service [1992].[1]

Francis: Yes. And in an editorial I just wrote for American Journal of Public Health.[2]

Hughes: Referring to the CDC again?

Francis: Boards of health--keeping the separation between public health and politics.

Political Interference with CDC

Hughes: Is CDC doing that?

Francis: No, it's terribly politicized still.

Hughes: Is that largely because of AIDS?

Francis: Largely, I think. Well, also because of some of the other issues. First thing Reagan did was disband all of our family planning people--no more abortion surveillance; that went straight away. NIOSH, the National Institutes of Occupational Safety and Health, got cut to hell. Anything that might interfere with business or promote abortion got chopped instantly. In all the governments I'd worked in around the world, I had never seen anything as repressive as the Reagan and Bush years--just terrible.

Hughes: So CDC hasn't bounced back from the Republican administrations?

Francis: No, it will take years to bounce back.

I'll give a local example. No more than three, four years ago, on International AIDS Day on December 1, the California Office of AIDS decided to have a display in the main building of the California State Department of Health Services in Sacramento.

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[1] Donald P. Francis. Toward a comprehensive HIV prevention program for the CDC and the nation. Journal of the American Medical Association 1992, 268, 11:1444-1447.

[2] Insulating public health from extremist politics. American Journal of Public Health, May 1994, vol. 84, 5:720-721.

And the director said, "I hope you don't have any condoms there." This was years into the epidemic, when condoms were the foundation of AIDS prevention programs! And notice that the CDC came out with MMWRs on condom efficacy and needle exchange efficacy only after the Clinton administration came to power. The data on their benefits existed for a long time, but CDC never dared to publish them during the Reagan and Bush years.

Hughes: Well, you said last time, that one of the reasons you left the CDC was lack of resources. But Shilts mentions policy differences between you and Jim Curran as a reason. Shilts' point is that Curran took an epidemiological approach where you took that of a vaccinologist wanting control of the disease.[1] Is there truth in that, and could you talk about those different approaches to an epidemic?

Francis: There is some truth to it, exaggerated no doubt in the movie.[2] In general, Jim and I worked well together. His interest was a little more academic than mine. I have great academic curiosity, but when it comes to an epidemic, my job is to respond. Maybe it's because I came into CDC through the Epidemic Intelligence Service, which was this epidemic training program, and he came in through kind of a postdoctoral study program. His interest was research, but that was very complementary to mine in disease control. If he wasn't interested in intervention, he had enough business to do in research for a lifetime. So we were quite compatible if I were more interested in prevention than he was.

Our boss, Dr. Walter Dowdle, asked me to put together a national AIDS prevention program, which was fine.[3] Jim was not interested, and I was, so I did that. Ultimately the plan went up to Washington for funding and was totally shot down.

Hughes: On what basis?

Francis: Money. $37 million a year. For the United States of America.

Hughes: Do you think that was the total issue?

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[1] Shilts, And the Band Played On, pp. 482-483.

[2] "And the Band Played On"--A Home Box Office (HBO) film based on Randy Shilts's book by the same title, broadcast in September 1993.

[3] Donald Francis, James Chin. The prevention of acquired immunodeficiency syndrome in the United States: An objective strategy for medicine, public health, business, and the community. Journal of the American Medical Association 1987, 257, 10:1357-1366.

Francis: That was certainly the first step. I think the rest of it was, who cares if these guys die.

Hughes: That response was what caused you to leave Atlanta?

Francis: That was it. That was what sent me to California.

Failure at the Federal Level

Hughes: Well, I have a quote from Don Francis about government ineptitude: "The worst thing in all this, which I only came to recognize as the years went on, is that the government had no concept of what its role should be in an epidemic."[1]

Francis: That refers to the federal government's role, the upper levels of government, the Reagan administration. CDC was in the epidemic business--that's the Center for Disease Control. It's up to its ears in epidemics all the time. I think when you get to be very specialized, you tend to assume that everyone around you has the same specialty knowledge that you do. By that time, we had become so knowledgeable and specialized that when we started talking about AIDS control, people really did not understand what the hell we were talking about. I didn't recognize that. I didn't recognize that there was a knowledge and experience gap.

Hughes: Which people didn't understand?

Francis: The blood industry, the administration, whomever. Therefore, some of our mistakes were marketing failure and upstream management failure. But, in addition, some didn't care to listen to us anyway.

But the administration had no idea of what their responsibility was as a government. Second to national defense, public health is one of the major priorities of government, and has been since our founding. A society better have sewers and immunizations and do whatever else you need to in public health, otherwise people die. They had no concept of this at all. The policy of the Reagan administration was, no government was better government.

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[1] Steve Heilig. Donald Francis, M.D.--How CDC politics has botched the fight against AIDS. California Physician 1992, July:38-41.

Hughes: Yet, in the history of public health, there has always been a quibble about how responsibility for public health should be divided among different branches of government, and particularly, where does it become the states' responsibility?[1]

Francis: In the early seventies, when I was actually assigned to a state, and we were starting to get some good health officers out in county and state levels, many of whom came through the CDC training programs, the system worked reasonably well. For any given disease, the narrow expertise was at CDC, and some at state health department level, and then general public health was at the local level. And by and large, the regulatory power is with state and local health departments.

If CDC, if the federal government felt there was a very important epidemic, be it immunizable diseases, be it tuberculosis, be it sexually transmitted diseases, then federal money would come down with some rules on its use, so the program would be designed federally but with considerable local autonomy.

That worked very well--not perfectly, no doubt--because, frankly, local authorities sometimes have very little flexibility due to their lack of resources. Their tax base is very limited. States, a little bit less so, but still not like the federal government, which can come up with billions and billions by shifting resources. Our tax structure is very federally oriented. This typically decentralized U.S. approach was not perfect in any way, but it was workable.

With the AIDS epidemic, the CDC should have taken its traditional, strong, federally funded leadership role, performed the essential research using its technically expert people, and sent that information and money out to the state and local health departments. Usually CDC assigns people much like me to help deliver these programs. There should have been someone like that in every major state. As a matter of fact, there should have been at least three physicians, one in San Francisco, one in L.A., and one at the state level in California--that would have been typical CDC response in the past. CDC sent me to Bareilly, India, (as a WHO medical officer) to head up a district smallpox program. That's a long way from Atlanta, but we felt that if we got rid of the disease there, we wouldn't have a problem here. It was a very smart move.

The system can work, but what happened with the Reagan administration compounded the difficulties of responding to a new

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[1] See, for example: Sandra Panem, The AIDS Bureaucracy, pp.37-38.

epidemic. They cut back local funds for multiple programs. What happens at the local level, unfortunately, is when poor people get sick, they go to the hospital, and they cost money. Those costs must be absorbed by basically a fixed budget. With less federal support, less health insurance from business, more poor people coming to public hospitals, more local money is going to have to go to the hospitals. But the health budget at the local level includes public health. And when the health demands increase, everything else has to decrease if you're going to keep your tax burden the same.

So what happened in those years when the federal government was cutting back money and the AIDS epidemic was growing, the health care budget was just eating everything else up. Prevention programs and the ability to support preventive medicine at the local levels was eaten up even more. This at a time when we had a weak federal government, an impoverished local government, and the state somewhere in between. It was a setup for disaster.

The Epidemic's Personal Impact

Hughes: You have been in this epidemic now for over twelve years. What sort of impact has it had on you as an individual?

Francis: Well, it's not the field that you'd recommend a young public health person to get into and make their name. It's a difficult and often unpleasant field. But I had already done great things. I had eradicated smallpox; I felt really good about what I'd done The hepatitis stuff was marvelous, and some of my other work, like Ebola, was great. So I was old enough to look at AIDS as an education, and it was a marvelous if not always pleasant education. I got to know some really good people in the world--in the community, in politics, and the upper levels of government.

Equally important, there are some real bastards. And you can't ignore those bastards; you have to deal with them. And you may lose. You have to be very clever, because evil people are often very clever. But the whole political process of bringing opposing forces together and getting support to outdo the evil was an education I would never have had without AIDS. So dealing with the ugliness was valuable.

Hughes: What are you thinking of specifically when you say that?

Francis: Ronald Reagan and his entourage, Bill Dannemeyer and his ilk--these almost fascist-type people who seem to be well-meaning but do evil, evil things. We can't sit back and let them run the show, or you'll have a really bad society.

I guess next I've learned it's extremely hard for humans to work together. They are, especially the male of the species, basically designed to fight. The future of our society depends on our ability to harness that aggression, which was, no doubt, useful during 99 percent of our evolution, for killing mastodons and fighting off incurring tribes and such. Yet it's not very useful any more. It seems more common to fight than it is to work together and compromise and move ahead.

I'm not sure if I'm optimistic or pessimistic for the future. The thing that saddens me is to see the tremendous potential that we have in this world that we let pass; the beauty that we have in this area of California, and still we can't build transportation facilities, for example. We can't deal with getting people from here to there and plan long-term and realize what that does to the quality of life. I think we're close to useless at planning the long-term.

So that realization has really depressed me and bothered me. Yet I'm basically an optimist and think humans have an amazing strength to come through in the end. I guess I've also realized you have to have a crisis to get people to change. I think that's terrible, because people get tired of having crises.

AIDS has been very hard on my family. My wife has been remarkably tolerant, but not always, and I think basically she hates AIDS, because it's taken me away from the family an awful lot. She is a professional who has been trying to do her career, and I was always in the lab, in the field, or on a trip or somewhere. She recognizes that I have an inherent characteristic that makes social good take precedence over individual good, and I sometimes sacrifice the family for the society. I sacrifice myself for the society, which she as a mother cannot understand. She will sacrifice herself for the kids, me for the kids. There's no doubt in my mind who would stand first. That's been tough.

But I don't think I'd trade it. I would rather surround myself with some nicer people sometimes, but it's been a marvelous experience. Where else but at CDC could you do all those things I have done? In twenty years, I did a dozen things that most people wouldn't be able to do in a whole lifetime. So I wouldn't trade it, even though it was hard.

I guess the last thing is, I hate death. I had to deal with my parents' deaths, and patients' death, and I just hate death. Maybe that's one of the reasons I went into preventive medicine. And I hate having all my friends dying. God awful. I still have Stan Hadden's [State Senator David Roberti's staff] card in my Rolodex, Randy Shilts' card in my Rolodex, and I don't know if they'll ever come out. I can't adjust to their absence. I guess I plan to call them when I need them...

Hughes: What do you think the CDC thought of your effort in the epidemic?

Francis: Oh, I think they respected it. The CDC is a wonderful organization underneath. They gave me awards, and Jim Curran gave me a box of donuts. [laughter] No, I think there's a lot of mutual respect between both CDC and myself. Maybe some of us have different styles, but I think all of us had the same endpoint in mind, and all of us were very disturbed that CDC was so badly damaged. CDC is incredibly important--it's an international jewel. You destroy that organization, and the health of the world suffers. There ain't many places in the world like CDC.

The Epidemic's Impact on Medicine

Hughes: Would you comment on the ways in which the epidemic has impacted medicine?

Francis: Oh, it's had huge impact, all the way from the old issue of individual doctors treating patients with infectious diseases to the rapid application of the most modern laboratory techniques to day-to-day patient care.

Hughes: What do you mean by the old issue of infectious diseases?

Francis: Infectious disease were thought of as being things of the past. This epidemic has certainly brought infectious disease back to the front page. Interestingly, most of us who go into infectious disease do so because patients come in very sick and go home very healthy very quickly, or they die. It's a specialty that does not center around chronic conditions very often. AIDS changed that. Also the poor dermatologist who went into that field to take care of healthy people with pimples got a rude awakening with AIDS, just like the infectious disease folks. That's why a lot of AIDS care is managed by oncology services instead of infectious disease services.

AIDS has politicized all of medicine. What the AIDS activists did with AIDS women now want to do the same with breast cancer. You'll see more politicization of health now. It certainly drove a lot of things to the front--the health care financing issue. We can't do public health unless somebody takes care of health care financing. So it has helped pushed that to the fore. I could go on and on and on.

We must realize that with all of its problems, the epidemic has been important to medicine, and it's brought a lot of new faces into public health. I wouldn't have thought of myself working with the CMA in years past, but they are a great organization in many ways, and really have the right approach to medicine. It's brought practicing physicians together with public health like never happened before.

Hughes: Why were you reluctant to work with the CMA in the past?

Francis: In the sixties and seventies, I thought the AMA [American Medical Association], because of its social stands, was one of the worst institutions in the world. As a result, I have never joined the AMA.

AIDS and Cofactors

Hughes: Do you want to comment on the suggestion that HIV needs a cofactor or cofactors?

Francis: Of course it needs a cofactor; all infectious diseases have cofactors.

Hughes: Well, in the Duesberg sense.

Francis: Duesberg speaks nonsense. Peter Duesberg has lost the ability to honestly look at scientific data and adjust his understanding. He ignores scientific facts. Warren Winkelstein and I sat down at lunch with Peter Duesberg at the Women's Faculty Club at Berkeley and almost got kicked out, because Warren and I became so frustrated. That fellow could not understand that being HIV infected was a bad thing. He wanted to infect himself with HIV to show it was benign. He is a biochemical virologist who's trying to understand epidemiology and infectious disease, and he cannot make the leap and does not understand the complexity. He has by and large lost his scientific integrity, the respect of others, and probably some psychological sanity. He's ridiculous.

Cofactors are involved. But regardless of all the cofactors such as age, genetic makeup, and whatever foreign proteins you've got circulating around, if you take HIV away, AIDS goes away. You put HIV in and it comes back. That's all I need to know. I don't even know why some people get so sick with measles and some people don't, or why some people get sick with chicken pox and others don't. Of course there are cofactors, but God, you take chicken pox virus away, and there won't be any chicken pox. The bug is the essence.

Heterosexual AIDS

Hughes: The recent report on AIDS from the National Research Council emphasized that the epidemic is not democratic; it strikes socially and economically marginal communities with greater force.[1] What are the implications?

Francis: It's true. One of the silliest things about the AIDS epidemic is that somebody could write a book about the heterosexual myth of AIDS, and have it published, and people read it. The expectation of this virus coming into every automobile going down the freeway is just naive. If you understand the epidemiology--it's sexually transmitted; it's blood-borne; the more sexual contacts you have in a community, together with some cofactors, including genital ulcers that increase the risk, then you'll have more disease [in that community] than you would elsewhere.

We know that there are groups in society that have more risk behaviors than others. That's where the virus is going to concentrate. Simple as can be. So if your expectations are it's going to spread rapidly into every corner of society, then you will be disappointed. The expectation was false; it is going to dribble out, but not explode. There's no way that you can keep HIV limited to any community. Why does the daughter of a General Motors executive get infected with HIV? It's because her contact was part of a riverlet which joined one community to another. He got infected and gave it to her. So there are going to be these riverlets of infections in every community. That's what happens with infectious diseases.

In the past in public health, or even today, if we have one importation of a virus that has a mortality rate of even 10 or 20

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[1] The Social Impact of AIDS in the United States. Washington, D.C.: National Academy Press, 1993.

percent per infection, we blow all the whistles in public health and make sure it doesn't go anywhere. This one [AIDS] has a 90-plus percent mortality, and we're saying, "Well, there aren't too many heterosexual cases. Only 5,000 women a year come down with AIDS." Wow! I call it the body-bag phenomenon. We just get accustomed to this incredible misery and say, "Well, that's not too bad. Only 1 percent of African Americans in Oakland are infected with this virus. That's a lot better than 50 percent of the gay community." That's a stupid way to look at it. If 1 percent of the African American heterosexuals in Oakland are infected, you better do something.

I tell you, from having teenage kids and talking with mothers of other teenagers, if there were a vaccine for HIV, every mother would get it for their kid. They may say, "It's not my problem." But they also say, "I don't want it to be my problem, either." Under the surface, there's a much more logical response to this than meets the eye. At least here. Because everyone around this part of California knows somebody who's died of AIDS.

Hughes: Yes. But we're not living in--

Francis: Average Nebraska.

Hughes: You've talked for something like six hours. Is there any record that you want to set straight, or anything you want to add?

Future Issues

Francis: I think the most important thing is to look ahead to the future. The first issue for me right now is vaccines,[1] and frankly, our free-market society is not designed to develop vaccines. In many ways, we don't value prevention. Thus vaccines are bad business. So a small group of us limps along trying to make a vaccine, even for North America and Europe where there's a large potential for profit. It's still not as potentially profitable as a Tagamet or Tylenol, and thus it is seen as a relatively poor business opportunity.

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[1] Dr. Francis retired from the Public Health Service in February 1992, and began to work at Genentech to develop a vaccine for HIV. He currently heads Genevax, a company spun off from Genentech in 1996, which is focused on HIV vaccine research, development and testing.

We've got to change that model, even for this part of the world. For the developing world, there will never be a vaccine if we don't do something about it. Why would Genentech make a vaccine for Africa? Just out of the goodness of their heart? They could take this whole company, sell it, and buy vaccine for Africa and still not have enough, and have a company that's totally bankrupt. So something has to be done to change that model. In many ways, it's similar to what we have been talking about for six hours. There are some issues that don't fit well into our current system yet are socially very important to deliver--rapid transit, public health, et cetera--a nonprofit or government institution has got to take responsibility for these.

I would like to get across that individuals make the difference--whom you elect, who is your health officer. Those who account for a difference in a specific area are often five or ten people for the whole country. We have to have a garden where those people can really grow and not be stultified. That is going to require some chaos and environments where a few people can gallop ahead and make progress. By and large, our systems don't do that. They tend to support those who seek the status quo. The status quo for many of these issues, like AIDS, must be declared unacceptable.

I hear some very good cooks in this area that I have great respect for saying, "I will not have recombinant tomatoes in my restaurant." Well, our agriculture, and our dogs, and our cows, have all been selected by genetic selection. This may not be by genetic engineering, but by just selecting and breeding. Luther Burbank did a lot of early research on breeding of flowers.

We've got to be able to accept, and indeed desire, change for the good. Some of the technology can be dangerous, but a lot of it is not. We've got to be able to look at scientific data and translate it into good. That requires an incredible educational level so that people can read newspapers and understand the issue. And I don't think we've got enough of that capability at this point, including for AIDS. We only get interested when it blows up in our faces. When a mortar hits the market in Sarajevo, we get concerned. But next week when there's no mortar, we won't be interested, and those poor people are in there in the midst of some primitive, tribal fighting, and we do little to bring civilization back to them. Africa is being eaten up by tribal warfare, and we're just going to watch and let it die.

Another lesson: AIDS came from deep, dark Africa, way back in the jungle somewhere. It got to the United States like that--[snaps fingers]--once the ecology was set. And the next bug is

sitting out there now, somewhere in the world. The world is much smaller than it ever was before. I've been in the most distant parts of the world with some of the most dangerous viruses, and I know that someone who was in contact with one of these bugs the day before he left is in London right now. And that's the way it is. There's no part of the world that we can ignore.

It has to be a world family, and we have to deal with these sorts of things. But we don't seem to want to, especially Americans. We're so insulated, because we live in such a lovely place, wealthy, isolated from the rest of the world. Immigration will eat us up if we don't. You can't stop the world's poor from coming in here, because the economies elsewhere are so weak. Let's make the economies there better so that we don't have that kind of a stress.

So the smallness of the world has to be stressed. We are all in the same village, and we'd better take care of each other. That's all.

Hughes: Thank you.

Transcribed and Final Typed by Shannon Page

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The San Francisco AIDS Oral History Series

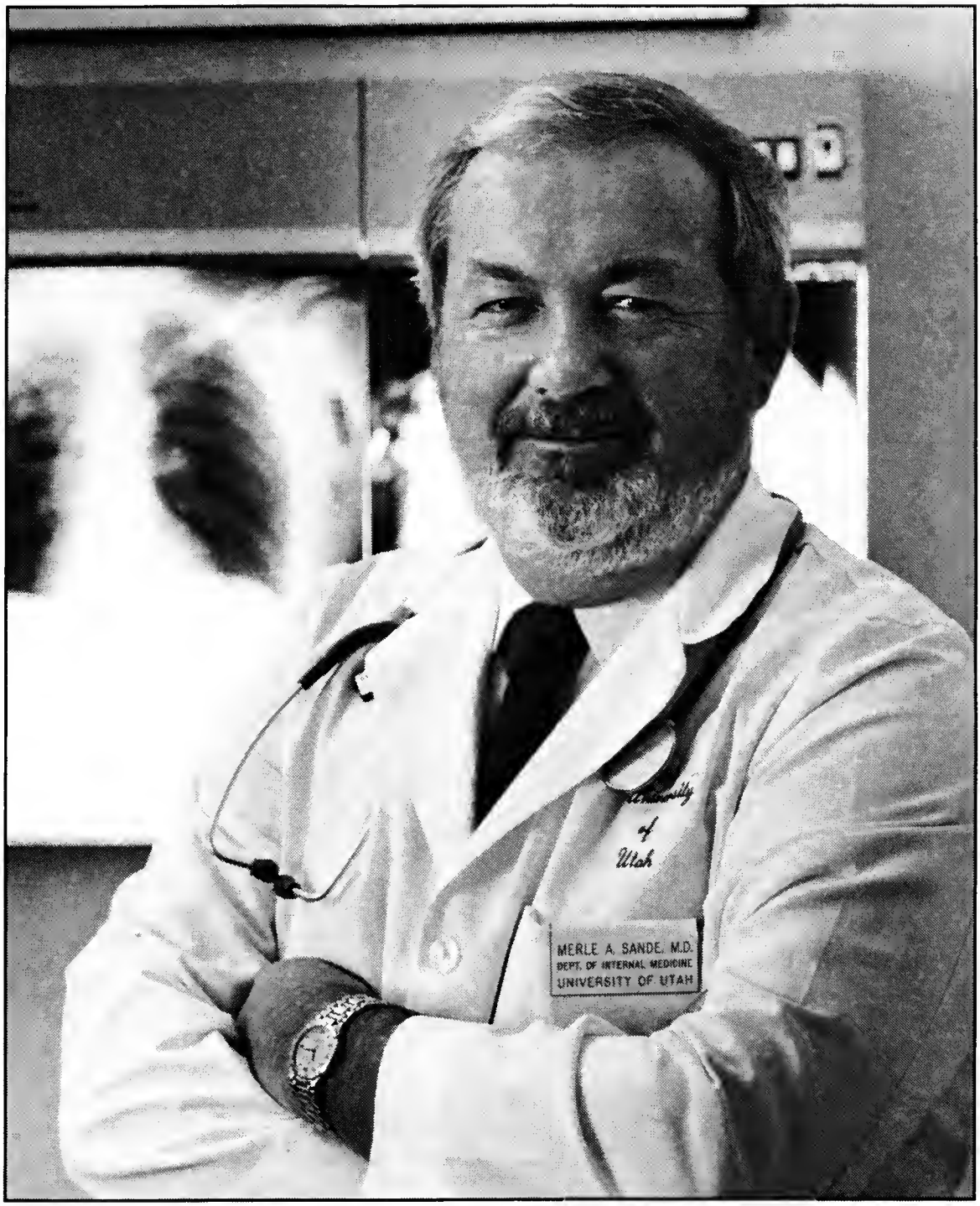
THE AIDS EPIDEMIC IN SAN FRANCISCO: THE MEDICAL RESPONSE, 1981-1984

Volume IV

Merle A. Sande, M.D.

INFECTIOUS DISEASE SPECIALIST: AIDS TREATMENT AND INFECTION CONTROL AT SAN FRANCISCO GENERAL HOSPITAL

Interviews Conducted by
Sally Smith Hughes
in 1993 and 1994



Merle A. Sande, 1996.

Interview History--by Sally Smith Hughes, Ph.D.

Dr. Sande was invited to participate in the AIDS oral history series primarily because of his role as the senior administrator at San Francisco General Hospital [SFGH] most directly involved in the institution's response to the AIDS epidemic. In September 1980, he arrived at SFGH as the new Chief of Medical Services, a position to which he brought career-long experience in infectious disease. His job as chief of medicine was, as he succinctly put it, "to bring this place [SFGH] into national prominence." [p.198] The following spring, the first cases of what later became known as AIDS were described in San Francisco and elsewhere. Such cases were at first of only passing interest to Sande who as a key player in a complex institution administered by both the city health department and the University of California had multiple demands on his time. There was no way he could have then suspected that the epidemic was going to be a vehicle for bringing prestige to the institution and to many of those, including Sande, involved with it.

One of Sande's first recruits was Paul Volberding, who in the summer of 1981 became head of the new oncology unit at SFGH and co-director, with Marcus Conant, of the Kaposi's Sarcoma Clinic at UCSF. These units saw many of the earliest AIDS patients in San Francisco. As an infectious disease specialist, Sande was aware of some of these troubling cases and in fact describes in the oral history a case of toxoplasmosis which he tentatively dates to the spring of 1981.

By 1983, the situation had changed. The trickle of AIDS patients had become an avalanche. As chief of medicine, Sande was not only involved in formulating policy to handle an unforeseen number of patients with strange and usually fatal conditions but also to stem the fear of a hospital staff dealing with an infectious and fatal disease of unknown etiology. The formation in 1983 of a clinic and inpatient ward dedicated to AIDS was one of the hospital's major responses to the epidemic. Another, which Sande describes at some length in the oral history, is the formation of infection control guidelines erected for the primary purpose of protecting hospital staff. In March 1983 Sande was appointed head of a committee, the UCSF Task Force on AIDS, which, despite its comprehensive name, was focused on devising guidelines for the safety of staff dealing with AIDS patients. Its heated deliberations resulted in publication in the fall of 1983 of an article on infection control in the prestigious New England Journal of Medicine.

Perhaps because of this publication, and the fact that the task force was composed largely of physicians, it somewhat eclipsed the work of the hospital's long-standing infection control committee which had been attempting, before Sande's task force was formed, to address disease-transmission problems presented by the epidemic.[1]

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[1]For an account of the history of early infection control guidelines at SFGH, see the oral history in the AIDS nurses series with Grace Lusby.

Sande was also chairman of the UC Systemwide Task Force on AIDS, a committee formed in 1983 to distribute California state funds for AIDS research and which continues today as the Universitywide AIDS Research Program. In 1984, Mayor Dianne Feinstein appointed him chairman of her Mayor's Advisory Committee On AIDS. Sande's three committee chairmanships served to give him visibility and influence in university, city, and state AIDS politics. Such standing was doubtless helpful in the skirmishes involved in establishing the Gladstone Institute of Virology and Immunology at SFGH. This achievement not only abetted the institution's AIDS research efforts but also complemented Sande's intent to reenforce it as a site of basic as well as clinical research, and as a rival of its sister institution on Parnassus Avenue.

But Sande is not all politics and prestige. The oral history reveals him as a man who has learned a lot, professionally and personally, from his involvement in the epidemic. His views about medical education and a physician's responsibility to his patients have changed as a result.

> ...I think we [physicians] have become much more sensitive to quality-of-life issues, of dealing with the human part of the patient. I think [AIDS] has brought the art of medicine back into our medical education process. The idea of orchestrating a good death, which would have been an oxymoron in my days of training, has now become a real endpoint (p.193).

The Oral History Process

Three interviews were conducted with Dr. Sande between September 1993 and January 1994 in his office at SFGH. Although pressed by the heavy demands of his position, he was nonetheless willing to take time to reflect on the early years of the epidemic. After a period of reminiscence off tape, he entered the discussion with a seemingly new-found sense of immediacy for the period we were about to address. When he asked how frank he should be, I urged him to be so and assured him that he would be asked to review and correct the transcripts. He replied that he wasn't worried, and as the first interview progressed appeared to relax and warm to his memories, positioning his feet on the edge of his desk and answering reflectively and sometimes eloquently. One suspects that he is an inspiring teacher and leader. Before the final interview, we took time off tape to reconstruct the chronology of Dianne Feinstein's Mayor's Advisory Committee on AIDS, which first met under that title on October 22, 1984. We decided that it was a formalization of an earlier informal set of mayoral advisors, which included Marcus Conant and Paul Volberding.

Sande reviewed the edited transcripts, making no substantive changes. In June 1996, Dr. Sande left SFGH, doubtless proud that once again an annual survey of U.S. hospitals had judged it to provide the best AIDS medicine in the country. He is currently chairman of the Department of Medicine at the University of Utah.

The Regional Oral History Office was established in 1954 to augment through tape-recorded memoirs the Library's materials on the history of California and the West. Copies of all interviews are available for research use in The Bancroft Library and in the UCLA Department of Special Collections. The office is under the direction of Willa K. Baum, and is an administrative division of The Bancroft Library of the University of California, Berkeley.

Sally Smith Hughes, Ph.D.
Research Historian

Regional Oral History Office
April 1997

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 Merle Alden Sande

Date of birth September 2, 1939 Birthplace Washington

Father's full name Sigvald Sande

Occupation _____ Birthplace _____

Mother's full name Clara Sande

Occupation _____ Birthplace _____

Your spouse _____

Occupation _____ Birthplace _____

Your children Suzanne, Cathleen, Eric, Sarah

Where did you grow up? Washington

Present community _____

Education B.S. Washington State University

M.D. University of Washington School of Medicine

Occupation(s) physician

Areas of expertise Infectious diseases

Other interests or activities golfing, hunting

Organizations in which you are active _____

I FAMILY BACKGROUND, EDUCATION, AND EARLY CAREER

[Interview 1: September 21, 1993] ##

Early Education

Hughes: Dr. Sande, let's start with where you were born and educated.

Sande: I was born in a little town north of Seattle called Mount Vernon. It's a small farming town. My parents [Sigvald and Clara Sande] were first-generation Norwegian immigrants. My father worked on the Stern wheeler boats up and down the rivers in the Northwest, and then became involved in the Washington state ferry system. For about thirty-five years, he was skipper on the ferries that ran from the state of Washington to Victoria, where I worked for a number of years with him.

I went to Mount Vernon High School [1953-1957]. From high school I went to Washington State University [1957-1961], where I was interested in physical metallurgy and engineering. I got talked into taking some zoology courses, and got interested in medicine. Then at sort of the last hour I decided to go to medical school. I was concerned about that, because I could never stand the sight of blood.

Medical School, Internship, and Residency

Sande: I went to the University of Washington School of Medicine [1961-1965], and always had interest in going back and practicing family practice in my own little home town. I was told by Bob Petersdorf, who was chairman of medicine then, that that wasn't what I should do, that I should become an internist. So he sent

me then to New York Hospital at Cornell for my [internship and residency] training [in internal medicine] [1965-1969].

Hughes: Why Cornell?

Sande: He had a way of selecting the top five people in the class and orchestrating their careers. So he said, "Sande, you go to New York Hospital," and I said, "Yes, sir."

So I took my wife [Mary Ann] and my two young children, and we went off to Manhattan, which was quite an experience for us--small-town boy in the big city. But it wasn't bad, because we were on [duty] every other night for four years, and we never got to see anything anyway.

Interest in Infectious Diseases

Sande: I finished my internal medicine training in 1969. I had an interest in infectious diseases, although I never took a fellowship. Even though I'm currently the president of the Infectious Disease Society of America, I'm sort of a fraud.

Hughes: Why infectious diseases?

Sande: It was the most exciting thing that we did in medicine. They were the most interesting diseases. They were the ones that you could do something about; you could make a definitive diagnosis. I think those of us who had sort of a surgical mentality but found themselves in medicine wanted an end result to something, and I think a lot of us were attracted to infectious disease.

But also it was the mentoring. Mentors have tremendous influence on the way you make decisions about your career choices. My mentors there, fellows by the name of Don Kaye and Ed [Edward] Hook, were both very stimulating. And Petersdorf, chairman of [medicine? at] the University of Washington, from my medical school days, was also [in] infectious diseases and maintained an interest, a tie with us. So I became interested in that area; did a little investigative work while I was still a resident.

Then, during the height of the Vietnam War, I got assigned, happily, to Lackland Air Force Base [San Antonio, Texas], where my first year I ran the general medical clinic, and then the second year I became an infectious disease attending at Wilford Hall Hospital and did part-time work at University of Texas Health Science Center, San Antonio. That was where I really got into the

more academic aspects of infectious diseases. I still had interests in 1970 of going back to the state of Washington to practice medicine.

Faculty Member, Division of Infectious Diseases, University of Virginia School of Medicine, 1971-1979

Sande: By that time, my mentor at Cornell, Ed Hook, had become chairman at University of Virginia. He enticed me to come back East, and I went to Charlottesville [1971-1980], where I started actually in family practice and medicine, again working in the general medical clinic, but also having my academic research interests in infectious diseases. So my career in academic ID [infectious disease] really started in 1970. I went up the academic scale to professor, and then to acting chairman of medicine in 1979.

Hughes: At Charlottesville?

Sande: In Charlottesville, at the University of Virginia.

My research interests were developing animal models of infection so we could study various organisms (bacteria and fungi) in models of endocarditis and meningitis. That's probably what I was most known for before I came here.

Hughes: The use of animal models was a standard way of studying infectious disease?

Sande: Yes. My philosophical approach to infectious diseases was to try to find out how things that happened in the test tube with bacteria and antibiotics correlated with what actually happened in the animal models. There is often times a big difference between things you see in broth and things that actually happen in vivo. So we essentially developed animal models, usually using rabbits, where you could create situations and study the in vivo effects, which then are very directly related to patients. So I tried to bridge the gap between the test tube and the patient by the development of the animal model.

We were extremely successful over the years, in terms of making significant observations--why certain diseases develop, particularly bacterial endocarditis, what the factors were that influenced the development of those diseases. And then in the field of meningitis, we designed the model which is used all over the world now. I did this with a fellow by the name of Ralph Dacey, who was a medical student with me and now he's chairman of

neurosurgery at Washington University at St. Louis, a very creative young fellow.

When I was there [at the University of Virginia], I had a lot of fellows who are still close to me, and who have now distributed themselves around the country and around the world. But I think my major interest was always in teaching and using infectious diseases as a prototype for general internal medicine as a whole.

Professor of Medicine, San Francisco General Hospital, University of California, San Francisco, 1980-1996[1]

Recruitment

Sande: I actually looked at a job in San Francisco in the mid-seventies as chief of infectious disease here at San Francisco General Hospital [SFGH], and decided to stay in Virginia. I looked at a couple of other jobs, but then when this job, as chief of the medical service at San Francisco General, came up, it was perfect. It fit my interests. It's a sort of hospital that I enjoy working at, and the quality of the people on the housestaff was such that it was a really nice fit.

So I came here in September of 1980, having had a year of really good experience running a big department of medicine in Virginia when Ed Hook went on sabbatical. So I was, I think, pretty well prepared for this change.

It was a very traumatic year, because I was here five days when the housestaff went on strike. It had been brewing. It was a time of a lot of chaos and instability, at UC and at San Francisco General. But it passed.

The Setting at San Francisco General

Hughes: Well, talk about the staff that was in place when you arrived, and what the facilities were.

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[1] In 1996, Dr. Sande moved to Salt Lake City to become chairman of the Department of Medicine at University of Utah.

Sande: At that time we were not very strong in infectious diseases, and that was one of the reasons I think I was recruited here. But we had a lot of space. It was these old buildings that had been used as hospitals before. The new hospital had opened, I think, in 1978, so the old hospital building that was here had been torn down. But the other hospital buildings around the area were preserved almost as historical monuments. So that offered a chance to build research labs and research institutes.

Hughes: Which was one of the things that had appealed to you?

Sande: Yes. The thing that has made us what we are today, which is the number one public hospital in the country bar none, in terms of any way you look at it--research grants, faculty, whatever--was the availability of the initial space, and tremendous vision by two people: Holly Smith [Lloyd H., Chairman, UCSF Department of Medicine], and Julius Krevans [Dean, UCSF School of Medicine]. And there were a lot of others who had a part, but those two really had the vision of turning San Francisco General into a highly visible, recognized, credible extension of UCSF. It's not an ancillary hospital; it is as important to UCSF as the Parnassus campus is, in terms of research grants, in terms of teaching, and everything else. It's one of the songs that I sing over and over again.

Hughes: Had there been much of a research emphasis prior to your arrival?

Sande: Well, there had been a stable group of investigators who had used the County [SFGH] as a base of operations. Some of them, like Y. [Yuet] W. Kan, had left here and gone over to UC. He's now a [Howard] Hughes [Medical Institute] investigator as one of the giants in the field of molecular biology, probably one of the fathers of molecular biology. Most of the investigation taking place here was clinical investigation. There was some basic science, but there wasn't a lot.

Now, I was recruited just a year after the Gladstone Institute for Cardiovascular Disease opened [1979], and that was the first major step of enticing private money into San Francisco General. Bob Mahley was the head, and still is. He's just been very successful. Then, a whole series of recruitments followed. There was the Rice Liver Laboratory that Monty [D. Montgomery] Bissell ran in the department of medicine, and that's been very successful. About the same time I was recruited, Ira Goldstein was recruited from NYU [New York University] to run the Rosalind Russell Arthritis Institute.

Within a couple of years, the [Ernest] Gallo family gave money to start the Gallo [Clinic and Research] Center, and Ivan

Diamond was recruited to run that. Then a year or so later, with the help of Jay Nadel and others, the Lung Biology Center opened. Joe LaDue was particularly influential in raising money, and that's been extremely successful. So there's a whole series of these things that happened that allowed us, a poor city hospital, to develop an incredible basic and clinical science environment.

What I was offered when I came here was really nothing except a vision, and Holly Smith, who recruited me, said, "Look at all that space. Now you go out and fill it."

Hughes: He meant with research activities?

Sande: Yes. We had the clinical activities. This has always been a very strong clinical training program.

Hughes: Is that somewhat related to the city's diverse population?

Sande: Yes, the clinical training program is good because of the patient population, because it's one-third of the UCSF program, which has a very good program in internal medicine, and because there is a cadre of very committed and dedicated clinicians who work here. I think they make a happy environment, a pleasant place to work, although our patients are not always pleasant patients to deal with--the intravenous drug users, the alcoholics. The overriding spirit of clinical care is just outstanding, and it always has been.

Hughes: I understand that the atmosphere, the spirit, here is really quite different from that on Parnassus.

Sande: Yes, I think so. I take great pride in that, because I think that's one thing that has made this place a really productive and fun place to work. I think there is a sense of family--a sense of family maybe because everybody here considers we're working in the battlefield, and we're closer because of the environment and the patient population that we serve. But I think there's also been a sense of family in terms of sharing our accomplishments and feeling a part of a vibrant, growing community. Success breeds success, and success is attractive and it tends to draw people into a shared sense of responsibility. I think that's happened. It's been a remarkable fourteen years.

Hughes: Do you think that would have occurred regardless of the epidemic?

Sande: I think so. AIDS has only been a part of the story. The epidemic created a new arm of the hospital that was initially primarily focused on clinical investigation, and then more recently has been focused with the new Gladstone Virology Institute on basic science

investigations. But overall, the contribution that we made in AIDS was mostly clinical more than it was basic, while most of these other institutes [at SFGH] were doing basic research in other areas, not related to AIDS.

Increasingly, we try to tie them together, because if you study AIDS and you understand AIDS, you really understand an awful lot about human biology and human disease. As that's become more recognized, the barriers between disease states have broken down, and it gets down to fundamental biology. AIDS is an incredible opening of basic knowledge. Using the virus as a probe has increased our understanding of how the immune system works and how cells are turned on and turned off. It's an explosion of understanding.

II THE AIDS EPIDEMIC

Preparation for the Epidemic

Hughes: Do you have anything to say about retrovirology?

Sande: I didn't know what a retrovirus was.

Hughes: [laughs] A lot of people didn't.

Sande: Remember, my background is in infectious diseases, but it was in bacterial and fungal infections and not in virology. I think that we've all become pseudo-retrovirologists; at least we now know the language.

One of the neat things about this environment is that you can't help but learn what's going on, because there's so much going on around us that, if you attend the seminars or listen to people or interview people for jobs, you learn what's going on. Retrovirology is one of the more common topics that we discuss. And it really has been quite remarkable how studying AIDS has helped our understanding of molecular biology, genetics, cell biology, cancer, immunology, and other infectious diseases.

Hughes: Is there anything we should talk about before my next question, which is how did you encounter the AIDS epidemic?

Sande: Well, I think that it's been written and said a lot that it was a perfect marriage for me personally, having had a background in infectious diseases, and to have gained a certain level of prominence or credibility in the field, to be at the same time chief of medicine at the hospital in which it really all first happened. It was lucky for me. I think it was fortunate that I had a way of thinking about diseases that had an infectious orientation, that it was a good marriage to be here when the epidemic happened.

First AIDS Patient

Hughes: Tell me how you first became aware of what later was going to be known as AIDS?

Sande: I've thought about this a lot. The first patient I saw--my dates are always sort of suspect these days--in the spring of '81, was a patient on the fourth floor with three brain lesions--a young gay male. We had biopsied him three times, and we couldn't figure out what it was. Finally, somebody thought they saw toxoplasmosis. We sent the specimen down to Jack Remington at Stanford, and he confirmed that it was toxoplasmosis.

Hughes: He being an expert?

Sande: Jack Remington is an expert in toxoplasmosis. He was also a good friend. That [case] was really bizarre; it didn't make any sense, but we see a lot of bizarre things.

Hughes: So you didn't think too much of it?

Sande: I didn't think too much of it.

Then Paul Volberding, whom I had recruited in the middle of '81--he's one of my first recruits, actually--to come over from the Parnassus campus and run our oncology service here at San Francisco General, told us about some of the KS patients that he was seeing with Marcus Conant in the Kaposi's clinic at UC.[1]

Then, I remember a rumor came from the CDC that they had seen a cluster of gay male patients with an unusual pneumonia in Los Angeles. The report by Mike Gottlieb at UCLA came out in the MMWR [Morbidity and Mortality Weekly Report] that summer of a cluster of five patients with this weird pneumonia called Pneumocystis. At about the same time, we started seeing patients here with Pneumocystis pneumonia and we were off and running.

Hughes: Did you make connections between patients at SFGH and those elsewhere?

Sande: Not until the Gottlieb report. It really didn't register. We were seeing the Pneumocystis pneumonia cases, but they didn't make any sense. They were all in gay men. The toxoplasmosis patient was gay. The patients with Kaposi's sarcoma were gay. But it was

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[1] See the oral histories in this series with Drs. Volberding and Conant.

the click from the Gottlieb observations that, "Gee, there's something really bizarre going on here."

Hughes: What was clicking? The fact that all this was happening in gays?

Sande: Yes. See, that didn't make any sense. Then you said, "Why would a gay male be different? Why would they be developing these diseases?" Particularly Pneumocystis that had only really been seen in very young undernourished children, or patients undergoing cancer chemotherapy, or who were on high doses of corticosteroids, who had immunosuppression.

So then the thoughts were, Well, there is certainly no evidence that gay men were genetically different. There were some theories that perhaps through their sexual activity they were getting large doses of different antigens, and somehow these antigens were turning on one part of the immune system, and maybe suppressing another part of the immune system. There was some suggestion that maybe the parasites that they were acquiring were immunosuppressant. There was some data to suggest that the sperm itself might be immunosuppressant, so perhaps gay men who were experiencing very promiscuous behavior might be developing an immunosuppression that set them up for opportunistic infections and malignancies. But nothing really made any sense.

Infection Control

Initial Concerns

Sande: One of the personal observations that I had, that I will never forget: It became obvious that this disease or condition was infectious. It was clearly obvious to me that we, in this hospital, were the most exposed, because by that time we had had more [AIDS] patients than anybody in the country, as far as we knew. My training in infectious diseases was actually probably a hindrance, because I really got worried. I said, "My god, I'm responsible for this group. I'm the responsible person for this housestaff and these nurses, for the faculty, and I am an 'infectious disease expert.' So what should my responsibility be?"

I remember very clearly 1952, when three of my best friends got polio in the summer. Do you remember this? It was a tremendously scary situation--

Hughes: Yes, the swimming pools were closed.

Sande: We couldn't go swimming. My mother would ask me every morning if I had a stiff neck. And it was that fear of the unknown. I had exactly the same feeling with AIDS. Suddenly one night, it just hit me. It really was scary, and very uncomfortable.

Hughes: What convinced you that the other theories were probably wrong, and that it was an infectious agent of some kind?

Sande: I don't remember what the precipitating event was. In '82, IV drug use was recognized as a vehicle. Then Diane Wara with Jay Levy and Art Ammann described transfusion AIDS, and then AIDS in children.[1] Transfusion AIDS didn't really fit some of the earlier noninfectious theories for immune deficiency. [tape interruption]

So then we started thinking about what could it be that would cause this immunodeficiency in that group of patients. The only thing that made any sense was that it was infectious. If it was infectious, then how was it transmitted? If it was not culturable and it was small, it's a virus, and how are viruses transmitted? When you think of viruses, you think of influenza and you think of chicken pox and you think of measles, and you think of things that are rapidly transmitted through aerosol and through coughing and through touching and through secretions.

This is where I was in an incredibly unique, singularly unique, position. I was the one responsible. I had more [AIDS] patients than anybody in the world. I had a faculty, nurses, students, housestaff, that were incredibly exposed. And that scared the hell out of me. It really scared me.

UCSF Task Force on AIDS

Hughes: Another factor, I should think, was that your staff was afraid, as I learned from interviewing them.[2]

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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.

[2] For example, see the oral histories in this series with Donald Abrams, Andrew Moss, and Paul Volberding.

Sande: Yes. And so that's what precipitated the first dean's committee [UCSF Task Force] on AIDS, which was started in '83.

Hughes: Yes, March, '83.[1]

Sande: I chaired that committee [1983-present], and that was a very interesting group of people.[2]

Hughes: It was called the UCSF Task Force on AIDS, but wasn't it initially conceived pretty narrowly as an infection control committee?

Sande: Yes. Initially, [Julius] Krevans actually called me and said, "What do you think about this epidemic?" I said, "Well, I'm sort of worried about it." So he appointed me to put together a group to think about it, and to try to get a real heterogenous group of people. It was a wonderful group--Merv Silverman, the health director, came to all the meetings. Initially I guess Geoff Lang and then Phil Sowa, our hospital administrator, came. The head of nursing [Mary Anne McGuire] came. We had Fran Streiker who was from the West Bay Hospital Association, because they were starting to see AIDS cases, and the West Bay Hospital Association was worried about what we were going to do. We were obviously in the driver's seat and needed to do something.

Hughes: These people were actually made committee members?

Sande: We made them committee members. Marcus Conant was part of the group. And Paul [Volberding] was vice chairman. Then the infection control people, John Conte.

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[1] H. Baine Fairley, Associate Dean, to Merle Sande, February 7, 1983. (AIDS History Project Archives, Special Collections, UCSF Library, Ward 86 papers, carton 1, f: to PV [Paul Volberding], 1983.)

[2] Acting School of Medicine Dean Robert Credé appointed the UCSF Task Force on AIDS in March 1983, a campuswide committee charged with developing AIDS-related infection control guidelines. In July 1988, the task force was disbanded when Chancellor Julius Krevans established the UCSF AIDS Coordinating Council, an advisory group of faculty and staff at UCSF and its affiliated programs at SFGH, Mount Zion Medical Center, and the Veterans Administration Medical Center. Many individuals who had served on the UCSF Task Force on AIDS became members of the Coordinating Council. (Dianne Leiker, UCSF AIDS Coordinating Council: Historical Report [n.d., probably 1988], binder: AIDS Coordinating Council: Historical Report, AIDS Coordinating Council Office, UCSF Faculty Club.)

Sande: Keith Hadley, from infection control here. There's a really long list of people.[1] And Connie [Wofsy] and Don Abrams became part of it.[2]

Now, one of the complicating features was [SFGH surgeon] Lorraine Day. I brought her on the committee, because she was starting to agitate about the fears and the problems with HIV. She took my comments and made slides out of them, "So-called AIDS expert says, `Health care workers not at risk,'" which is not what I said, but that's what she put in her slides.

Hughes: Can you remember when you appointed her to the committee?

Sande: No.

What was very interesting is that we really knew we had to make some guidelines, and in a way, I guess, we were lucky, because we didn't know that the incubation period of this virus was ten years--incubation period meaning disease from period after infection. Had we known that, we would have been more concerned. In '83, two years into the epidemic, there really hadn't been any health care workers that had developed AIDS from taking are of patients--even people who had been working extensively with people with AIDS.

Reports of Low Infectivity

Sande: One thing that really helped us in the decision was a couple of the family studies came out. They suggested that if there was a child in the family environment with AIDS, that the other siblings or the parents didn't get it. So we said, "It really must not be very infectious or contagious from casual contact."

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[1] See the oral histories in this series with Drs. Wofsy and Abrams.

[2] For members of the task force as of fall 1983, see J. E. Conte, Jr., W. K. Hadley, M. Sande, et al., "Infection control guidelines for patients with the acquired immunodeficiency syndrome (AIDS)." New England Journal of Medicine, 1983, 309:740-744.

Hughes: Yet there were some scares. Remember the [James] Oleske household contact scare and an accompanying editorial in JAMA [Journal of the American Medical Association] that fanned the fear?[1]

Sande: Yes, it did, it was open. And I wrote the editorial[2] for the New England Journal of Medicine article that Rogers and Friedland published. They had published on a group of people from Montefiore [Hospital in New York] who had household contact with people with AIDS, yet they didn't have any evidence of transmission in family units. So I wrote the editorial, saying, "It looks to me like AIDS transmission is not going to be a big problem in hospitals."

There was a fear, because we didn't know for sure. And you know, you're not sure, in retrospect, if you made the decision based upon just the facts you had or if there wasn't some impact of wishful thinking in the final decisions. Pragmatically--and this is what Lorraine has been most critical of me for--we had this large group of patients to take care of. Who's going to take care of them? So given the pressure of caring for the patient population, and then looking at the lack of cases in people that did care for them, and the lack of transmission in that family setting, we just said, "Look. People have to be rational, and we have a major responsibility as health care workers and particularly as physicians to give this care. We might be missing something, and there might be a risk here, but right now, we can't see it."

Then there was that nurse in England that got infected with a needlestick. Then we started focusing much more on needles.

Julie Gerberding and the AIDS Health Care Workers Study, 1983-present

Sande: By the way, that was Julie Gerberding who just looked in here, and Julie was the person who was working with me as a resident at the

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[1] J. Oleske, A. Minnefore, et al. Immune deficiency in children. Journal of the American Medical Association 1983, 249:2345-2349; A. S. Fauci. The acquired immune deficiency syndrome (editorial). Journal of the American Medical Association 1983, 259:2375-2376.

[2] M. A. Sande. Transmission of AIDS: The case against casual contagion. New England Journal of Medicine 1986, 314:380-382.

time who took on AIDS infection control, and now is the world's authority in that area.

Hughes: Her study began in 1983, didn't it?

Sande: Yes. We started collecting blood specimens.

Hughes: How was that study set up and conducted?

Sande: Well, what academicians should do when faced with an unanswered question, a clinical dilemma, a clinical problem, is they should start accumulating information. We should start saving specimens and documenting exposures. Julie was going to be chief resident the next year, taking a year off after she finished her residency, and she was actually working at Kaiser. So she submitted a grant application to the statewide AIDS task force [Universitywide Task Force on AIDS] that I at that time [1983-1988] was chairman of, and they funded her to set up a health care workers' study.

So she started accumulating clinical data and blood specimens from health care workers and their patients from whom they got a needlestick. She then collected serial samples. Over the years she has documented over 1,000 such accidents and has documented transmission in one episode and perhaps one other.

Hughes: The specimens were blood?

Sande: Yes. With that information and with the clinical history and the characteristics of the needlestick, she was able with a great deal of credibility to say, "Well, HIV infection from a needlestick does happen, and this is the risk. The hospital is not a zero-risk environment." Well, it's an enormous risk if it's you, or if you work for the EPA [Environmental Protection Agency]. It's a very small risk if it's somebody else, and you're looking at transmissibility, or you're using hepatitis B as an example of high infectivity. Hepatitis B is about a thousand times more infectious than HIV.

Because Julie had started early and saved specimens, she was able to make the statement about relative infectivity before anybody else could.[1]

Hughes: Was anyone else doing this sort of research?

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[1] J. L. Gerberding, C. E. Bryant-LeBlanc, et al. Risk of transmitting the human immunodeficiency virus, cytomegalovirus, and hepatitis B virus to health care workers exposed to patients with AIDS and AIDS-related conditions (ARC). Journal of Infectious Disease 1987, 156:1-8.

Sande: The CDC was trying. They were trying to pick up cases from around the country.

The UCSF AIDS Task Force Infection Control Guidelines, 1983

Sande: The infection control guidelines that we finally came up with in this committee were incredibly good.[1] But in some areas, we agreed to disagree. The issues weren't just infection control. The issues were care of patients with AIDS. We talked about the right to refuse to care for patients with AIDS--under what circumstances there should be a right--and we figured there were essentially none.

Hughes: Is that based on the Hippocratic Oath?

Sande: Yes. We said that if you're a physician and you're in this setting, and somebody comes in who's sick with HIV, then it's your obligation to care for him. Actually, Molly Cooke, who was on that committee, was very helpful in terms of the ethical dilemmas that we faced.

Hughes: Had she some background in medical ethics?

Sande: Let's see, by that time, Molly was doing a Robert Wood Johnson fellowship and had been interested in medical ethics. She had been my chief resident in 1980 and was still involved with patient care at SFGH.

Anyway, after we had come up with all these recommendations and we synthesized scenarios and responses to scenarios, I called my friends at the CDC. At the other end of the line were Jim Curran and Harold Jaffe and Jim Hughes.

On the conference call, I read them our recommendations, which were very bold and brave for that time. We agreed that we didn't have all the information necessary to be sure that our

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[1] J. E. Conte, W. K. Hadley, M. Sande, and the UCSF 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. See also, Report from the UCSF Task Force on AIDS, June 2, 1983. (Binder: AIDS Coordinating Council: Historical Report, AIDS Coordinating Council Office, UCSF Faculty Club.) For other perspectives on infection control at SFGH, see the oral histories with Grace Lusby and Cliff Morrison, AIDS Nurses series.

statement was true, but this was the best we could come up with at this time. It looked like casual contact was not going to transmit whatever this thing was, that needlesticks may be a problem--you had to be careful with them; you should use good infection control guidelines, but that we didn't think that it went beyond that, and you should take care of these patients, and you didn't have the right to refuse.

Hughes: There was controversy about whether employees who were immunocompromised should be allowed to take direct care of patients.

Sande: Yes, that came later.[1]

What was interesting about that conference call [with the CDC] was there was a dead silence when I was finished. They said, "Well, Merle, why don't you publish it, and we'll react to it." [laughter] Beautiful bureaucratic response. So we went ahead and published our infection control guidelines, and they were very important and accepted.

Then we revisited it--Julie really did--a couple of years later, and we made some minor changes.[2] Once the virus was isolated they knew what was causing it. We had guessed right.

Hughes: Did the CDC endorse the 1983 guidelines?[3]

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[1] At a meeting of the UCSF AIDS Coordinating Council in November or December, 1988, Julie Gerbering discussed the need for a UCSF campuswide policy for, and a system for dealing with, health-care workers exposed to HIV-contaminated secretions or other materials. [Minutes, AIDS Coordinating Council, n.d. but between 11/18/88 and 12/20/88.] The question of what to do about employees exposed to HIV through needlesticks was an issue at least as early as 1983. (See, the undated, unattributed document, Recent Questions Regarding the Care of AIDS Patients and Handling of Specimens and Instruments, Marcus Conant's KS Notebook for 1983.) The interviewer was referring to a discussion in 1983 by members of the UCSF Task Force on AIDS on whether hospital workers with AIDS should be allowed to provide direct patient care. [David Perlman. UC Hospitals' guidelines on AIDS cases. San Francisco Chronicle, June 3, 1983.]

[2] J. L. Gerberding, UCSF Task Foce on AIDS. Recommended infection-control policies for patients with human immunodeficiency virus infection: an update. New England Journal of Medicine 1986, 315:1562-1564.

[3] The CDC had issued infection-control guidelines in November 1982. (MMWR 1982, 31:577-579.) For a discussion of the CDC guidelines and those of the SFGH infection control committee, see the oral history with Grace

Sande: Not officially, but more or less.

Hughes: Did other institutions adopt the guidelines?

Sande: Yes, I think everybody finally came along to the same conclusion. But I think we clearly broke new territory with that.

Hughes: Did you have to get approval from the Department of Public Health, or could you just go ahead and publish and establish these guidelines?

Sande: We don't work for anybody. We have total academic freedom. The dean told us, "Do the best job you can." He didn't know anything about it. So no, we didn't have any approval from anybody, except everybody signed off on it who was on our committee, which included Merv Silverman, who at that time [1983] was head of the Department of Public Health.

Hughes: Well, is there a point when other guidelines come in, from OSHA [Occupational Safety and Health Administration], for example?

Sande: Over time, I think that our recommendations were the ones that carried the OSHA standards and everything else.

The Infected Health Care Worker

Sande: Now, you brought up another issue, which is a much more current issue, really three or four years ago, and that was the infected health care worker. That's been a very tricky one. The new committee, which is the Chancellor's Task Force on AIDS, which I continue to chair, made a very strong statement that we felt that there was no justification for screening health care workers for HIV, or if it became known that they were HIV positive, for benching them from their clinical activities, that the data didn't support that.[1]

Hughes: There wasn't enough evidence that indeed they were a significant risk?

Lusby in the AIDS Nurses series.

[1] UCSF Policy for Health Care Personnel Infected with Bloodborne Pathogens, February 1991. (See binder: AIDS Coordinating Council Correspondence, 12/3/90-11/18/92. Chancellor's AIDS Coordinating Council Office, UCSF Faculty Club.)

Sande: Right.

Implications of the David Acer Case

Sande: This all became a problem after the Florida dentist case, Dr. Acer's cases. We became very close to the CDC and to Dr. Jaffe and the group, and they examined that epidemic and felt like there was reasonably good evidence that the virus came from the dentist. And of course, that conjured up visions of a dentist pricking himself with a needle and bleeding through his gloves into the mouth of the patient. And that never made much sense; theoretically possible, but not for five different individuals.

Now the data has been questioned, but I think more than the data being questioned, the mechanism by which that happened has been questioned. We've heard that Dr. Acer had Kaposi's sarcoma in his mouth, and he worked with his instruments on his mouth in the morning before he saw the patients, and didn't clean the instruments very well. That makes a lot more sense. Or the other really viable option is that this man was disturbed and did it deliberately. But we're probably never going to know for sure.

As a result of that one epidemic, there have been 20,000 or so lookbacks, and there's not a single case of transmission from an infected health care worker to a patient. And yet, it had such incredible appeal to the politicians, particularly to the right wing.

Our task force got together with the California Medical Association and the West Bay Hospital Association, and we had a press conference condemning attempts to test and restrict health care workers from performing their duties.

CDC Recommendations

Hughes: Any attempt to do mandatory testing?

Sande: We lost the fight, because the CDC did come out with recommendations,[1] but we won the war, because it's not going to be implemented, I don't think.

Hughes: What were the CDC recommendations?

Sande: Well, first of all, they had a list of procedures that infected health care workers couldn't do, and that was a disaster. They dropped that. Then they said, "Have the states come up with a plan, but they'd better be consistent with keeping the public safe from infected health care workers." Nobody's really responded to any of those things. It just sort of died down, went away.

The AIDS Outpatient Clinic, SFGH

Hughes: We skimmed over the inpatient and outpatient clinics. Let's go back. Can you start with the outpatient clinic, since that was first to open [January 1, 1983]?

Sande: Well, it was in '81, '82, when we first realized that we were going to have a lot of patients, and, as I said earlier, I had recruited Paul Volberding to come over and run oncology. He had an interest in Kaposi's. Then when we started seeing these new patients who had this immunodeficiency disease, mostly Pneumocystis but also other opportunistic infections, we thought that it might be worthwhile, since Paul was particularly interested in this, to expand the division of oncology to a division of AIDS and oncology. It was the first such division in the country, and I think it was important because it allowed us to give particular attention with a new division to a new disease. We put resources into it: we got resources from the city; we got resources from my department, and we hired some people--Connie Wofsy, Mark Jacobson, Connie Kaplan, Jim Kahn, and Donald Abrams--and we had a focused division.

We established a new clinic on Ward 86 initially, and so we asked Paul, "Why don't you start seeing the patients with this new syndrome there?" And again, it allowed us to attract resources from the city, saying, "Okay, here's a new disease. It seems to be occurring particularly in gay males. Let's concentrate our resources in this one area--in social services, the infusion center, all these other things"--sort of bringing the community

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[1] CDC. Acquired immunodeficiency syndrome (AIDS): Precautions for clinical and laboratory staffs. MMWR 1982, 31(43):577-580 (November 5, 1981).

into it. And that became the San Francisco model. It came out of this clinic concept of using the community resources, using the university resources, doing a lot of outpatient work, minimizing inpatient care.

Hughes: Was there a precedent for that model?

Sande: Not really. Not that I knew of. The thing that made the model work was the tremendous contribution and commitment of the gay community. Because you had people out there who were willing to donate their time and willing to work, bring people back and forth to the hospital, care for people in the home, all of these things. So it was real intense community involvement in the process, which probably could have only happened here, where the gay community is so tight and so involved. Paul was very good with the gay community, and with keeping people informed.

The AIDS Clinical Research Forum, SFGH

Sande: I established [1988] a group [AIDS Clinical Research Forum] for the activists that's never really gotten much publicity, but it was really effective. I would meet once every couple of months with the activists in San Francisco, and with Paul, John Ziegler, Mark Jacobson, Don Abrams, and all the AIDS investigators. We would present our research projects and the activists would react to them, and we would have a big interaction. That was really a successful group.

Hughes: This was entirely distinct from the mayor's AIDS advisory committee?[1]

Sande: Yes. We had the active people, Jesse Dobson and Martin Delaney from Project Inform, John James from the newspaper.

Hughes: AIDS Treatment News?

Sande: Yes. We had the lesbian groups; we had the Latino gay group and the black gay group.[2]

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[1] Sande was chairman from 1984 to 1987 of Mayor Dianne Feinstein's AIDS Task Force.

[2] Representatives of community-based AIDS organizations and physicians and other health care workers from SFGH and UCSF attended these meetings. By 1991, between thirty and forty individuals were receiving meeting

These meetings went on for a couple of years [1988-1991]. In fact, they were so successful that one day, Tony Fauci from the NIH [National Institutes of Health] brought his entire core of AIDS people--Dan Hoth, Jack Killen. They all came out here en masse and we met over on Ward 30 in the solarium. We had about a four-hour exchange between the activist groups and the NIH on the issue of clinical trials. It was really a good forum, because it was effective, and people had a voice.

Hughes: What sort of issues came up?

Sande: Mostly AIDS research and AIDS care, and how you're using your resources, and how you're doing your human experimentation, and how you're getting patient permission, and how you're getting access to drugs. We'd ask them, now what are you guys selling under the counter, and what are you bringing in from China? Because all the buyers' clubs were represented in the forum. So it was really an interesting exchange. This group proved to be a pivotal political force for a long time.

Political Involvement

Hughes: Were these meetings the beginning of the education of Merle Sande in terms of the gay community?

Sande: No. That happened a lot earlier. I got into the political arena actually in '82. Well, there are three areas where I've been very active politically at local and state levels. One was through the initial group that was advising the health director on the bathhouses [Medical Advisory Committee for AIDS]. Then the second one was the Mayor's Task Force on AIDS, which I really formed with Feinstein. The third one was the statewide AIDS body--what did we call it?

Hughes: Universitywide Task Force on AIDS.[1]

Sande: Yes. So those are the three areas where I had probably my biggest political impact.

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announcements. For the names of attendees, their affiliations, and other details, see the folder, AIDS Clinical Research Forum, in Dr. Sande's personal collection.

[1] The committee is now called the Universitywide AIDS Research Program; it distributes California state funds for AIDS research.

Medical Advisory Committee for AIDS, San Francisco Department of Public Health

Sande: The first one was a small advisory group that Merv Silverman established, and there were always at least five of us there--two from the gay community, two from the straight community--which was Paul Volberding and myself--and Merv Silverman. We agonized for a long time about the bathhouses and whether the health department should make an attempt to close them. It was very interesting. That's where I really got my education on the gay community.

Hughes: What do you mean when you say that?

Sande: We knew by that time--probably '82, '83--that the population which was becoming infected were the ones who had tended to have the most sexual experiences, the largest number of partners.

Hughes: Some of that evidence was coming from the health department. It was Selma Dritz's epidemiology?

Sande: That was part of it. But you know, it was also part of a report every morning here [SFGH], where you'd see these gay males, and they'd admit to large numbers of sexual partners in a weekend, and extremes of [sexual] activity. It seemed clear. Now, this is all, let's say, dataless impressions. But it seemed clear that those who were constant participants in the bathhouse activity were the ones that were being admitted to the wards with Pneumocystis pneumonia. And Selma's and Andrew Moss's initial observations fit with this. The number of partners seemed to be a risk factor, and particularly rectal receptive intercourse seemed to be a risk factor for acquiring HIV.

The Bathhouses

Sande: I remember saying at one of these meetings [of the Medical Advisory Committee for AIDS], "I cannot understand this resistance to closing the bathhouses. It looks like the data are becoming overwhelming, and it looks like this behavior is bad for your health." I was quickly informed that the freedom to express yourself sexually any way you want is something that the gay population had fought for for many years, and they were not going to give it up. And you know, I could understand that emotionally from their standpoint. I could not understand it medically. And physicians who were part of this group were making these points.

And Merv [Silverman] wanted to do the correct thing. He also wanted to do the politically correct thing. So he agonized a long time, and finally [Mayor] Dianne [Feinstein] got mad and fired him.

Hughes: But not until after he had closed the bathhouses [October 9, 1983].

Sande: Yes. It was an interesting process; it was an effective process, but it was too slow. It should have happened quicker. We knew that the actual closing wasn't going to really make a big difference, but the statement that we made was that we had thought long and hard about closing the baths, and this activity looked to us to be very bad for your health.[1] And you know, the judge reopened the bathhouses. But they died. They died because the evidence then became increasingly convincing that unprotected rectal intercourse with multiple sexual partners was very high-risk activity for transmitting the infectious agent responsible for AIDS (later found to be HIV). It was a very interesting time.

The Mayor's Task Force on AIDS

Sande: When Silverman was fired, I was made chairman of the mayor's task force [1984].[2]

Hughes: Why you?

Sande: I don't know.

Hughes: That must have been Feinstein's decision, right?

Sande: Yes. I don't know why. I was probably the highest-ranking university person involved. As head of all the AIDS activities down at SFGH, and independent of the health department but at least part of the scene, I was probably the logical person to do that.

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[1] For Sande's views on bathhouse closure see: Declaration of Merle Sande, M.D., October 6, 1984. In support of a temporary restraining order to close the bathhouses. Superior Court 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 1. See Appendix.

[2] The Mayor's Task Force on AIDS, also referred to as the Mayor's Advisory Committee on AIDS, was formed in 1984 after the bathhouse crisis.

Hughes: Do you think she wanted somebody independent of the health department?

Sande: Yes. I think she wanted somebody who wasn't directly responsible to her.

Hughes: Abrams, Volberding, and Conant were members of the committee at one time or another, and had UC connections.

Sande: Well, once they put it together, Connie Wofsy, Moses Grossman, Julie Gerberding, and Phil Lee joined the committee. Phil hardly ever missed a meeting. Then David Werdegar, who became head of the health department after I was made chairman of this committee. I'm trying to think. Flo Stroud.

Hughes: Who is she?

Sande: She's now acting head of the health department. Then Jim Foster, who was a health commissioner who died of AIDS, was there.[1] Also Andrew Moss, who probably made the most significant contributions to that group, because he was good at predicting the course of the epidemic. Do you know who he is?

Hughes: Oh, yes; I've interviewed him.[2]

Sande: Andrew was wonderful. Andrew had the vision before any of the rest of us did. He's always right. [laughs] Just amazing.

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Sande: He anticipated correctly the IV drug-abuser epidemic in the area. He predicted the tuberculosis epidemic, and now has spent the last year studying it in New York. He really was the one who taught us most about the risk factors that caused the transmission in gay males. So I think he, among all of the epidemiologists in the area, was the real hero. If I were to write a Band Played On thing, I would put Andrew Moss in there as the person who really understood the epidemic more than anybody else.

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[1] Representatives of Bay Area Physicians for Human Rights, the San Francisco Medical Society, Irwin Memorial Blood Bank, and community physicians in private practice also attended. (Minutes, April 23, 1983, San Francisco Department of Public Health, Irwin Memorial Blood Bank documents, binder 2, 1-5/83.)

[2] See the oral history in this series with Andrew R. Moss, Ph.D.

Hughes: Are clinicians likely to give as much credence to an epidemiologist as to one of their own kind?

Sande: Oh, yes. I don't think that's a factor.

Hughes: So there was no specialty rivalry?

Sande: No.

Mayor Dianne Feinstein

Sande: But you know, I wrote in, "The AIDS Epidemic: Blueprint of a Hospital's Response,"[1] that the relationship we had with Feinstein was absolutely magical. It was absolutely unique. Towards the end of her administration, we were meeting once a month with her. She really was hungry for information. She was the best-informed mayor in the country on AIDS, by far. Nathan Clumeck is a close friend of mine from Brussels. He was the first one to write a scientific article on AIDS in Africa, and it came out in the New England Journal in the mid-eighties. Within a week, I had him here, and he met with Feinstein to talk about what was happening in Africa.

Hughes: Meaning heterosexual transmission of AIDS?

Sande: Yes. Nobody knew AIDS was in Africa. He found that a lot of people from the Belgian Congo that came to Belgium were infected with AIDS, so he reported this. Warren Johnson, a good friend of mine from Cornell, was head of a clinical investigative program in Haiti. He identified Haiti as having a big problem with AIDS, and Warren came out and met with us. So we kept her abreast of what was new.

Hughes: When you say the relationship was magical, you mean in terms of access to the mayor?

Sande: Well, let me tell you. It was really interesting. Feinstein used us for a totally nonpolitical purpose. She used us for advice. She would come out with some of the most outrageous things, and we'd sit there and say, "You've got to be kidding me."

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[1] M. A. Sande. The AIDS epidemic: Blueprint of a hospital's response. Transactions of the American Clinical and Climatological Association 1987, 99:185-195.

We had no axe to grind; we were not working for her; she had absolutely no influence over us. We were ideal advisors. We had nothing to gain, we had nothing to lose, by saying what we thought was right. That's what was magical about this. We never went public with anything that went on in there. There was one leak once, and boy, she called me instantaneously, and we plugged it. But it was a place where she could freely express herself, and we could tell her to go to hell, that what she said was just ridiculous.

We had an incredible respect for her sense, her judgment. So she used us, and she would come up with these things, and we'd say, "That won't sell; that will sell," and she never, ever went public with anything we didn't agree with as a group. Now, individuals might disagree. But I just think that in facing something as explosive and new and confusing as AIDS must have been for the politicians, she used us as well as any group of experts could be used. It was really remarkable.

Hughes: How much was she driven by the knowledge that the gay population was not only a significant percentage of the city--I've heard the figure of 10 percent--but also a heavily voting percentage?

Sande: I'm sure she was driven by that. But the thing that was good about it is she did not put members of the gay community on that task force just because they wanted representation. She didn't use it that way. She wanted to do the very best job she could do. I'm sure it follows that that would be politically advantageous to her. But she did it in a way that she separated politics from advice. So there was no politics in the advice. It was strictly scientific data, as best we could put it together, and she used our judgment on a lot of those things.

I remember one time we made a statement about how something would appear if she went public with it, and she said, "You guys are more political than I am. I don't want to hear that; I want to hear what you think." Which was quite remarkable. It was a refreshing baptism to how good government could be if it was used in a nonpolitical sense, and she did that.

When she became chairman of the AIDS committee for the mayors in the country, she used us all the time.[1] So that was very positive. I was very impressed with her.

Hughes: I've heard Feinstein criticized by people connected with the epidemic because of her straight-lacedness on sexual issues. Putting it baldly, she didn't want these activities going on in her city. That was particularly apparent before the Democratic National Convention in San Francisco in '86 when she didn't want the message going out to the rest of the country that this kind of sexual activity went on in "her" city.

Sande: She was not a proponent of bathhouse activity, I'll tell you that. But I don't recall ever hearing her say that. I remember her being disgusted by the thought of the glory holes and those sorts of things. That certainly didn't appeal to her. But I heard it not from a moral standpoint as much as I heard it as a result of its facilitating HIV transmission.

Hughes: So can I conclude from what you're saying that her personal morality probably didn't have much effect on policy?

Sande: I think it did not. I remember vividly her expressing her morality in a very outspoken way. But the policies that were implemented never reflected that feeling. When she went public with something, it had been well tested on a number of people in our group. So who knows the motivations for things, but I can tell you that in my experience of her, that it was pretty well thought out and pretty well censored by thoughtful people before it was expressed.

The AIDS Clinic and Ward, SFGH

Formation

Hughes: Well, I haven't heard enough about the AIDS Clinic and ward.

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[1] Dr. Sande refers to the Mayors' Task Force on AIDS of the U.S. Conference of Mayors; Feinstein chaired the task force from 1983 until her resignation as mayor, January 17, 1988. (Information courtesy of Sally Osaki, Office of the Executive Assistant to the Director of Health, San Francisco Department of Public Health.)

Sande: Well, the clinic was developed because it was expedient to develop it. We had no high-falutin ideas about turning this clinic into anything more than a clinic, but it clicked. It really clicked, because it became a place where the gay community could commit themselves to their constituency and also to fight the disease.

Now, the ward was a little bit different. In reality, I started the ward, which was initially 5B and then became 5A, because I was worried. My initial vision for the ward was to make it an infection-control ward, to make it an isolation ward, to treat AIDS like tuberculosis. This was when we were going through this agony of writing our [infection control] guidelines. But we didn't really know how contagious it was. That's why we always had private rooms for patients with HIV. The initial development of the AIDS ward was to protect ourselves and protect other patients from what we thought was a contagious agent.

Now, that's not the way it was sold once it was--I mean, after the AIDS ward opened, and we had written our infection control guidelines, and we had decided that AIDS probably wasn't that contagious, and it became a center where every politician in the country and many from Europe would want to have their pictures taken, and we generated tremendous resources because of it, we looked like geniuses. It had nothing to do with that initially. We did it because we were scared. I did it because I was scared. And then everything else just flowed. We used words like, "Well, it was a great place to focus our resources, and we got the Shanti Project involved, and it was a great place to train housestaff, and it was a great place to take care of patients--" all those things flowed in. It turned out to be a very, very successful endeavor.

Hughes: You mentioned going to the city for funding. Who arranged the funding?

Sande: It was Feinstein, to the health department, to us for the AIDS program, and it still flows. She was putting up to $17, $20 million into AIDS from city dollars, unlike any other city in the country. We got out ahead of everything. She supported clinicians here; she supported the beds here; she supported nurses here. So a lot of that was her doing. It also helped being her advisors, because we could point out where the needs were, and she responded I think very appropriately. And it worked.

Hughes: Well, talk about what happened once a patient was admitted.

Sande: The San Francisco model that was developed in the clinic is because we wanted to minimize inpatient utilization. But say, for example, a gay male with a new interstitial pneumonia comes into

the clinic or is seen in general medical clinic or in the emergency room. The patient probably has Pneumocystis.

Now, a number of things along this line were just wonderful. Keith Hadley and his group in the clinical micro[biology] lab developed a new way to diagnose Pneumocystis through sputum induction. So that was done up here by Phil Hopewell and his chest service, and then microbiologists would look at the smear, make a diagnosis and initiate therapy. We developed a whole approach to management of Pneumocystis pneumonia.[1]

Coordinating the Clinic and Ward

Sande: Then maybe the patient would be admitted to 5A or 5B, and they'd get started on therapy. This allowed us to do a lot of clinical trials on new drugs for Pneumocystis. Patients would be picked up by the AIDS service; they then would be discharged and followed over on Ward 86, in the AIDS Clinic.

Hughes: Did patients also flow the other way?

Sande: Sure. A patient would come into the AIDS Clinic. One of the things that was interesting was that we hired a number of physicians to see just AIDS patients. The clinic started working a little bit too independently, so when they wanted to admit somebody, the communication between the outpatient service and the inpatient service was terrible for a while.

I hired this fellow from Portland by the name of Michael Clement, who was just a genius at interpersonal skills. He's a gay physician, a wonderful guy, and he solved that in spades. So then we realized it was important to have a clinician who was always associated with the AIDS ward. We don't have a specific housestaff team working on the wards, but we had an attending who was always around to help facilitate communication. That one issue focusing on communication was incredibly important to making it work. That solved a lot of the problems, so then communication between the ward and the AIDS Clinic became really good.

Hughes: Are you talking about communication along the lines of, are there beds to accommodate the people that are referred to the ward?

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[1] For more on the management of Pneumocystis, see the oral history in this series with Constance Wofsy, M.D.

Sande: Yes. As we talked about earlier, there was a time when there was a lot of fear about taking care of AIDS patients, and there was a stigma that the AIDS patient, just like the gay waiter, might be transmitting some awful thing. So initially we put the ward together as sort of an isolated unit, initially twelve beds, and then a couple of years later, twenty beds. These beds are reserved just for AIDS patients.

The AIDS Ward

Sande: Around the country, they were having trouble getting people to take care of AIDS patients. We left ward staffing open. It was a volunteer service. The staff got paid for it, but they volunteered to work on the AIDS ward. We always had a list of people who wanted to work on the AIDS ward. Because it was volunteer, they developed an incredible esprit de corps. There is a wonderful spirit.

It actually was a cause of some concern to other wards, because these people had a special spirit about them. As a result, they probably got more resources. And then every Sunday some gal from the community would bring in food, and then Elizabeth Taylor gave us a great big television set. Actually, she made rounds with me a couple of times here on the service. So they were special.

Phil Sowa, who was hospital director when we started this, was really a very supportive person with this. He and I thought one day we probably should start doubling up patients. One patient per room was the way we started, but we started it for the other reason [fear of infection]. So later we said, "It's not infectious between people; let's double up." So we had a meeting with the nurses, and the nurses said, "Absolutely not." We looked at each other and we said, "You know, this is not a fight worth having. You win."[1] [laughter]

Hughes: Why didn't they want doubling up?

Sande: Because they had developed a way of caring for the patients. For example, a family could come and stay in the room; they had cots in patients' rooms. It was a tradition, and [the staff was] proud of it, and they had taught it. They weren't going to let a couple

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[1] See letter, The Staff of 5A to Merle A. Sande, MD, April 15, 1987. (Ward 5A archives, unlabelled off-white file box.)

of yo-yos like Sowa and myself come in there and tell them they couldn't do it. It was very interesting. They won, and they deserved to win. It was a nice way also of letting them know that that's their ward.

Hughes: What happened to patients who needed to be admitted and yet there weren't beds?

Sande: They got put in the other wards. We have patients with AIDS all over the hospital.

Hughes: And that never caused a problem?

Sande: Occasionally, people who weren't gay, who had AIDS from blood transfusion, did not want to be on the ward. There was a stigma associated with it, but it was very unusual to have that happen. Usually there was such a nice spirit [on the ward] that they enjoyed it. It was very good care, and it made us famous. Famous beyond all imagination. You just couldn't quite believe it.

It's true what I said about politicians: They've all come through here, and to have their picture taken--guy who's head of social service in England, the secretary of state of Scotland, a whole group from the German congress. All through Europe, they all come over here to look at the ward. Jesse Jackson, all the presidential candidates, came through here. We got sick and tired of them after a while.

Hughes: Do they go home and, in some cases, establish something similar in their countries?

Sande: They did in England, very much so. They took a lot of the concepts. Yes, we've exported a lot of technology for disease care, for a lot of the San Francisco model, community involvement.

Holistic Treatment of AIDS Patients

Hughes: What could be done for an AIDS patient in the early days?

Sande: Well, even today, what can we provide? The AIDS patient is a very complex individual. It became known pretty soon that if you had Pneumocystis, you had a disease from which you were going to die in the next year or so. So there was tremendous emotional concern, emotional upheaval, in the individual, his family, and his friends.

The other confounding variable was oftentimes his family would not know that he was homosexual. So they not only would now find out that their son was going to die, but that he was gay. I remember an air force general who just could not accept it. So learning to deal with those issues was equally important as learning to deal with the medical issues.

Hughes: Who did have to deal with those issues?

Sande: We did.

Hughes: Everybody? Physicians and nurses--

Sande: Yes. The housestaff, and the nurses, and the attendings, and the social workers.

Now, I have always said, and I firmly believe, that AIDS for us medically has been an incredibly humbling experience, and we certainly learned the limitations of our technical medical abilities in this disease. But it's been a real positive in re-teaching us the art of medicine--very important, I think. We have learned to deal with death and dying. We have learned to deal with code orders. We have learned to appreciate much more than ever before the quality of life endpoints in our therapeutic interventions.

We've also learned, I think, and very importantly, to orchestrate a good death, which is a characteristic that is extremely important. My philosophical approach to teaching is that if you can orchestrate a good death, it is a tremendous success. If you can allow somebody to die with dignity, to die without pain, to die without being alone, and you as a house officer, as an attending, have been able to do that, you should be congratulated for it. You should be rewarded for it. It's not a failure to have somebody with this disease die. It's a success to have them die in a setting that you would appreciate dying in. Ten, fifteen years ago, you'd never hear us say that. It's "keep them alive at all costs."

Hughes: How much did this new attitude or approach originate from the patients themselves?

Sande: A lot of it did.

Hughes: You mean that they were demanding a pleasant death? Pleasant isn't the right adjective.

Sande: Yes. As pleasant as a death can be.

Hughes: In the early days, the very informed and articulate patient population must have influenced the course of medical practice.

Sande: Yes. Very well-informed. Usually excellent teachers for our housestaff. They knew a lot more about the disease and the drugs than a lot of us did. You learn to listen to your patients.

More on the AIDS Clinical Research Forum

[Interview 2: September 23, 1993] ##

Formation and Membership

Hughes: Dr. Sande, I believe you want to say more about the AIDS Clinical Research Forum.

Sande: Yes. This was a group that we established because Steve Morin, who was Representative Nancy Pelosi's person on health, very early in her term, or maybe before she even was in Congress, told us--actually told us through Rudi Schmid, who was dean of medicine at UCSF at that time--that there was a gap that we had not recognized between the activists, who were very powerful nationally, and our own investigators, a gap in communication and a gap in knowledge of what each group was doing. So I established this group that included Martin Delaney and John Jones and Jesse Dobson, who was the head of the ACT-UP group here. There were representatives from BAPHR [Bay Area Physicians for Human Rights], the Hispanic AIDS group, and the African American AIDS group.

We met for a number of years, and we presented to this group drug trial protocols that were in the process of being developed, so they had a chance to react to them before they went into action. Then we also reviewed results of drug studies that we were doing at the time, and got feedback. It was often an explosive meeting--it was a meeting that I just didn't want to go to, but we did. I just felt like there was always a lot of things to talk about.

[tape interruption]

It started in March of '88, and it went through '91.

Hughes: Why didn't you like to go?

Sande: Well, it's one I worried about, because you could never predict the issues and you could never predict the temperament. Occasionally it was a very hostile group which was frustrated and wanted us to do more. We talked a lot about issues of informed consent, the use of placebos, fast tracking, why aren't you doing more, why don't you get more patients, why are you slow on this? But it was good for us to hear it. The end result of it, I think, was a very positive thing--much closer relationships--and they did not feel excluded from the process.

Hughes: Did they cause you to change process, protocol?

Sande: Oh, yes, sure. Lots of things would be brought up about how you get an informed consent, and what should be the placebo. So hearing it from people outside of the system was actually very beneficial. You didn't like to admit it, but it was very beneficial.

Hughes: Give me an example of some of the things you changed as a result of those interactions.

Sande: It's hard for me to remember specifically.

Compound Q

Hughes: Was Compound Q an issue?

Sande: Yes, well, Compound Q was an issue during the entire time, because Project Inform with Martin Delaney was doing its own clinical studies. Actually, we were a little upset with him for not being very forthcoming with the data in those meetings.

Hughes: About their results?

Sande: About their results.

Hughes: Why would that be?

Sande: Oh, probably because he anticipated us being critical of the way the studies were being performed. We had minutes of those meetings, and I'm sure they're still available.

Hughes: I know that Michael McGrath was doing research here on Compound Q, and there was research going on under Delaney.

Sande: I don't have much hope now that Compound Q is going to offer any great advance in the treatment of AIDS. However, when Mike made his first observations in the test tube, it looked promising. I'm afraid this happens a lot; things that work in vitro don't necessarily make drugs that work in people. That's Q.

Hughes: What did the Delaney group think?

Sande: I don't know what's happened to them. We haven't heard much more about it in the last couple of years. I remember when the international AIDS conference was here [1990], I ran a panel with Martin Delaney, who presented some of his data, and Dr. Arnold Relman, who was editor of the New England Journal of Medicine at that time. There was a very hostile interaction between the two as to what made up good research and what didn't.

NIH Visitors

Sande: After about a year, I told Tony Fauci, who's been a very close friend of mine for thirty years, that we were holding this meeting with the community to discuss clinical trials and other issues of common importance. He got very excited and flew himself, Dan Hoth, Jack Killen, Peggy Johnston, and about three or four other people from NIAID [National Institute or Allergy and Infectious Disease] at the NIH out here for a single meeting with this group. Tony held court for about two or three hours, answering questions, because he was also interested in trying to establish communication with the activists. We had really the only functioning group that I knew about in which investigators and activists were working together in a single group.

Hughes: How was that meeting in terms of atmosphere?

Sande: I think Tony got what he wanted. He got a dialogue. I know as a result of that meeting, some of the people in this group had direct access to him, which nobody else did. So he established what he wanted to establish, and I think it worked out very well. That actually was, when I think about it, one of the more interesting things that happened organizationally.

Hughes: Was this the only place that such a group existed?

Sande: I'll bet it was, because our investigators are all members of the UCSF faculty. Now, there were people from the VA [Veterans Administration Medical Center]--John Ziegler; people from the Moffitt [Hospital]--John Greenspan, Jay Levy, Harry Hollander.

They would attend some of these meetings with us and our investigators here--Mark Jacobson, Sharon Saffron, Jim Kahn, Lorrie Kaplan, Connie Wofsy, Don Abrams, Paul Volberding.

We would have an agenda; we would have the studies listed that we were going to talk about; the activists would come prepared to criticize them and react to them. I think it worked out quite well, even though, as I said, it wasn't a meeting I looked forward to.

Defining AIDS

Hughes: Well, let's go back to the early years. I want to talk about how the disease was initially framed, which as you well know was as a gay disease. What difference did that initial definition make in the sorts of questions that you asked? What might you have asked if it had not been framed as a disease of gays?

Sande: It's an interesting question. The gay association for us I think was a positive, in that it polarized a very vibrant, intellectually stimulating, intelligent group of men to a disease that they took on as their own. The negative impact was obviously that homophobia, hidden or latent, became expressed. It unearthed that in areas around the city, but not nearly as much here as it did in other parts of the country. All the pent-up fears of homosexuality and latent homosexuality. "So now not only does this group of people have sexual practices that are difficult to understand, but now they're also potentially dangerous, now they have a virus that I can potentially get." This brought out a lot of pent-up emotions.

Hughes: Which you saw expressed here?

Sande: Not much. Much more from friends outside. Well, I guess for some groups in the city and city government, of business people, people who may have had a homophobic orientation to begin with, it became perhaps easier to express that prejudicial attitude. But for people like myself, who never had much interaction or experience with the gay community before I came here, the epidemic quickly forced me into the position of having to interact very actively with the gay community--which was a learning experience, and didn't always come easily.

We talked yesterday about some of the bathhouse activities and actions that we took. It seems to me that today we, the old boys of academic medicine and the heterosexual community, are much

more comfortable with homosexuality and the gay community, much more comfortable, to the point of it never enters your mind any more. Many of my faculty are gay; many of our housestaff are gay.

Michael Clement, who I mentioned yesterday was the person Paul and I recruited from Oregon, had talked many times of writing an article about the importance of having a visibly gay attending physician as part of your department, somebody who is a role model for gay housestaff and gay students, and somebody who is visibly proud to be gay.

Michael really was that, and was very visible and very proud to be able to help people. So I learned a lot from him, as I have from many of my other faculty.

Hughes: Did you sense that gay patients were also more comfortable if there was an attending or somebody on the housestaff who was gay?

Sande: I don't know; I'm sure it did. One of the reasons I'm sure that we were so successful in providing care to the population was that we had gay nurses and gay physicians who were part of the program. The interaction was never worth discussing, because it became very natural. It wasn't forced; it was just sort of a natural interaction. I feel that way today, that it's very much that way now.

Hughes: Are you aware of other institutions that had an atmosphere that was comfortable for a gay patient, and presumably also for a gay physician?

Sande: I bet it was unique. I think it was one of the things that allowed us to be so successful. It's really quite remarkable that a city hospital like San Francisco General that has always had a reputation for good care of the sick, but we're just a little city hospital, and yet we have emerged as the number one AIDS hospital in the world. That is remarkable, when you think about it. And I think all the things we've been talking about: the support from the administration, the support from our chancellor and [chief of medicine and] dean [Julius] Krevans, and Holly Smith and Joe Martin--the impact of the gay population, and the impact of the gay physicians and support of the gay community have been remarkable.

Hughes: How fully did you buy into the early framing of the disease as a gay disease? When did you begin to think that maybe that wasn't broad enough?

Sande: I don't think we ever consciously made this a gay disease, because the transfusion cases and some IV drug-using cases came after

that. It never was important to us that it was or wasn't a gay disease. We knew that the gay community was very supportive of our efforts, and very supportive of the gay population with HIV. That was important to us. But framing it as a gay or non-gay disease wasn't really relevant to our operation at all. Most of the patients were gay; some of them weren't.

There was a feeling in the community that it didn't want this as a gay disease. You certainly heard that. And I remember when David Durack at Duke, who was a good friend, suggested in the New England Journal that they call it GRID,[1] which is gay-related immunodeficiency syndrome, there was an outcry, and it's a good thing that didn't go through.

By the way, do you know who named the virus HIV?

Hughes: A subcommittee of the International Committee on the Taxonomy of Viruses.

Sande: Do you know who chaired that committee?

Hughes: [Harold] Varmus.

Sande: Yes. I said that in my talk. The HIV of V, the human immunodeficiency virus of Varmus.

Hughes: [laughs] I never thought of the V business. But the gay orientation must have been important to some people, because look at the early theories. The immune overload theory, for example--

Sande: But theories came and went every day. Before the virus was identified, new ideas emerged all the time about why this epidemic was happening. Let's say that we thought it was overload theory--too many antigens from previous exposures to sexually transmitted diseases. Well, too many antigens rectally or intravenously, there are still too many antigens. So the theory still was possible.

Hughes: The only one I can think of at the moment that wouldn't be plausible is the popper idea.

Sande: Yes, that didn't last long.

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[1] D. Durack. Editorial: Opportunistic infections and Kaposi's sarcoma in homosexual men. New England Journal of Medicine 1981, 305:1465-1467.

CDC Epidemiology

Political Pressure

Hughes: Well, I understand that CDC spent a fair amount of time trying to track that one down.

Sande: Well, the CDC was under political pressure to track everything down. Some of them were false starts, and some of them were good starts, which is what you'd expect.

Hughes: Political pressure from whom?

Sande: From everybody. Certainly political pressure from the right wing; political pressure from the gay population to track things down and try to find quick answers to complex questions.

Hughes: Are you saying that CDC was under pressure to explore every possible cause regardless of whether it was on the surface valid?

Sande: The CDC was under incredible pressure throughout, particularly in those early days, but even as recently as the outbreak from the infected dentist. But I think they've done a remarkably good job on essentially everything else.

More on the Acer Case

Hughes: How did the CDC handle the dentist case?

Sande: This is a personal bias, but it's shared by a lot of us, that while the CDC did a superb job in working up the epidemic, the final word, the final perception, about the dentist epidemic was incorrect. It's a very complex issue. First of all, we don't know the truth. We suspect that five and possibly six patients of the dentist became infected with the same virus the dentist had.

Hughes: I thought that was sure, that they'd done the nucleotide sequencing and it was the same sequence in all cases.

Sande: The sequencing is not a sure thing, but it's probably correct. The image that was created by the investigation and the early publications from this was that probably the dentist stuck his finger with a needle or something sharp, bled through his gloves into the patient's mouth, and transmitted the disease. Therefore,

all health care workers that do procedures that could possibly nick themselves should be tested and benched if they are positive. That's what came out of this.

Hughes: And that was the CDC line?

Sande: They were careful not to specifically say that, but that was the implication. And then there was a call for a list of invasive procedures that HIV-infected people could not perform. There was direct implication that this dentist had done that (transmitted HIV), therefore all HIV-infected health care workers should be considered a risk.

The premise is probably incorrect. If the dentist transmitted the virus to his patients, he probably did it by infected instruments, by contaminated instruments. We do know that he had Kaposi's sarcoma in his mouth. We also are led to believe now that he used the instruments in his office on his own mouth, he or his dental assistant, and that those instruments were not cleaned well. Now, rational people looking at the data are much more likely to feel that that was the mechanism of spread rather than accidental nicking of his finger.

The other hypothesis which has actually gained more popularity recently is that this was an angry individual who did it purposely. Now, nobody's going to be able to tell that. But this one incident led to more confusion, to more hysteria, to more prejudicial reactions, to more witch-hunting, particularly in less informed regions of the country, than anything else. Now, I'm not sure the CDC could have predicted that, but there were also, as I understand it, very strong political--not interventions, but fooling around with this thing by the politicians.

And as I understand it, (which is all hearsay), it was John Sununu, who was assistant to the president, Jesse Helms [senator from North Carolina], and Orrin Hatch, senator from Utah, who were the three big ones who interfered with the CDC's publications, made them shred one of their documents because it didn't go far enough, and tried to instill the right-wing version, which is that health care workers who are infected are bad, and are potentially dangerous. Therefore everybody should be screened and benched if infected. The CDC never recommended screening. But the politicians certainly had that in mind. So this was a very uncomfortable, unnecessary, and hysterically motivated part of the AIDS epidemic that will be a black mark on all of us. I think the CDC did their job but the politicians blew it.

Hughes: I think it doubtless had repercussions for what you were doing concerning infected health care workers in the UCSF AIDS Task Force. Am I right?

Sande: Yes. We fought with letters and media presentations that the data did not support the recommendations.

UCSF's Attitude Towards AIDS

Hughes: Although I have read, and my information comes predominantly from Randy Shilts' book,[1] that in the early days of the epidemic, the campus on Parnassus [UCSF] was pleased to move the bulk of AIDS activities over here [SFGH].

Sande: I don't know where Randy got all this. I am really flabbergasted by his perception of reality. I'm sure we all have our own perception of reality. As far as I remember--and I was the single person who was more involved in UC politics than anybody else in the state--I never once perceived that there was an attempt by Parnassus to unload AIDS patients here. In fact, if anything, it was just the opposite; they developed an AIDS clinic [Adult Immunodeficiency Clinic] under Harry Hollander, who was one of my chief residents. And I never sensed that there was any attempt, even early, to downplay AIDS, to export AIDS, because of the fear of developing the reputation of becoming an AIDS hospital. So much of this came out of the figments of people's imagination, and that was a low blow. I don't agree with that at all. I think probably I am the single person that has the most access to that information because I ran all those committees. It was an earnest attempt on all of our parts, including the administration at Moffitt, to find a compassionate, user-friendly system for caring for AIDS patients. That's just a bunch of baloney, and it permeates a lot of what came out of that communication [And the Band Played On], as far as I'm concerned.

The Kaposi's Sarcoma Clinic

Hughes: The KS Clinic at UCSF preceded the AIDS Clinic at San Francisco General by probably a good six months. The KS Clinic was up and

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[1]Randy Shilts, And the Band Played On: Politics, People, and the AIDS Epidemic, New York: St. Martin's Press, 1987. (Hereafter: Shilts.)

running by the summer of 1982. The outpatient clinic got going here officially in January 1983.[1]

Did the KS Clinic remain strictly a KS clinic? Did it see other problems associated with AIDS?

Sande: You know, I'm not really sure. You should talk to Paul Volberding because he was really involved in that clinic. The KS Clinic continued to function under Marcus Conant. Marcus Conant is a clinical professor of dermatology; he has a private practice clinic across the street and down a little bit from Moffitt Hospital, and he saw KS patients.

Hughes: Did it make a difference that he wasn't mainstream academic UCSF?

Sande: Well, Marcus Conant is in private practice. He was very influential in gaining attention for and sounding the alarm, probably more than anyone else, in terms of, "AIDS is a big problem, and you guys have got to get off your duff and do something about it." He's the one who went to Willie Brown and said, "Listen, Willie, we need money for research," and got it. Then he was the head of our center.[2] He donates his time to UC to do things like that.

Hughes: You're talking about the AIDS Clinical Research Center?

Sande: Yes, that the statewide task force [Universitywide Task Force on AIDS] funds.

Hughes: Did the KS Clinic die when the AIDS Clinical Research Center came into being?

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[1] A combined dermatology-oncology clinic, called the KS clinic, was established at UCSF in September 1981 for the evaluation and treatment of patients with Kaposi's sarcoma. (Marcus Conant to William Epstein et al., September 2, 1981. Conant's KS Notebook, 1981-2/82.) A formal AIDS clinic was established at SFGH in January 1983, although patients with KS and/or opportunistic infections had been seen previously in the oncology clinic and, beginning in November 1982, in a combined KS and OI clinic. For further information, see the oral history in this series with Paul Volberding, M.D.

[2] Conant was the first director [1983-1985] of the AIDS Clinical Research Center at UCSF. For more on these subjects, see the oral history with Marcus A. Conant, M.D.

Sande: See, I don't know that. I think the KS Clinic continued for a long period of time. Once the flood hit, the KS Clinic was no longer able to handle any more patients than they were handling.

SFGH and the Competition with UCSF

Sande: You have to understand one other thing which I think is very important about the difference between San Francisco General and Moffitt, and that is, we here are incredibly competitive. We saw AIDS, and we grabbed it.

Hughes: Competitive with whom?

Sande: With Moffitt. Now, this is one thing that I've been accused of, and probably correctly, that I was looking for something to really make this place [SFGH] great. AIDS came along, and here I was an infectious disease-oriented person. I had Paul Volberding, who was a wonderful facilitator, communicator, organizer. We just went with it. We tried very hard to develop the resources necessary through the city, through other agencies, to build, build, build the program down here, make it the best in the world, and we did. We were jealous of--we were not interested in giving a lot of what we had built to Moffitt Hospital. Even though we're part of the same group at UCSF, we live by our own family here.

Hughes: Were there people at Moffitt who would have been very pleased to have taken a piece of the pie?

Sande: Probably. Jay Levy was there; Harry Hollander was there; Diane Wara was there. They had their own programs. But we had resources; we had space; we had patients; we attracted more patients. So I'm saying this not to be self-serving, but to explain a little bit and react a little bit to what Randy Shilts was saying.

Hughes: That's why I asked.

Sande: We wanted this. So we went for it. And I do not think in any way, shape, and form, there was an aversion to it at Moffitt.

Hughes: Conant had been first on the scene, in terms of organization anyway--he got the KS Clinic going and then invited Volberding to come in. Do you have any sense that he felt left in the dust, so to speak, when AIDS activities became centered at SFGH? Certainly by 1983, that's the case.

Sande: Well, I don't know how Marcus feels. When I gave the lecture for Krevans' retirement, I named Conant as one of the real heroes.[1] He is one of the real heroes. I was in the process of describing my perception of how he interacts with the academic community, and he doesn't interact a lot with the academic community. He's in private practice, and he has a lot of obligations at the state level; he was co-chairman of the AIDS leadership conference that the governor appointed, and he's been very active in lecturing and teaching around the world about AIDS.

But it's not really his thing to run a center. He doesn't get paid for running the center. He donates his time. And so after a period of getting it started, it passed over to John Ziegler. Now, that center has never come to San Francisco General. That is still administered at Moffitt and the VA, and we're part of it, and Paul is part of it.

Hughes: Is that just history? It was started there and it's never been moved?

Sande: It is history because it went there first, and it actually went to Conant first. The center funded initially an AIDS tissue bank that John Greenspan kept at Moffitt[2]. It's been very successful. It accumulated serum and tissue from the very beginning, and it is available to all investigators throughout the country, and it's been very well used and well managed. It also supported some clinical studies. It has a little granting cycle where it provides $10,000 and $20,000 grants for investigators with new, creative ideas. It just has always been administered there, and it stayed there.

Community AIDS Physicians

Hughes: Has cooperation within the local medical profession been the tradition in San Francisco? Is it a place where there is less physician infighting than elsewhere?

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[1] Symposium in Honor of Chancellor Julius Krevans, M.D., on his Retirement, UCSF, May 19, 1993. For a draft of Sande's talk, see "Sande Presentation: Symposium in Honor of Chancellor Krevans." (Binder: AIDS Coordinating Council: Historical Report, AIDS Coordinating Council Office, UCSF Faculty Club.)

[2] For more information on the tissue bank, see the oral history in this series with John S. Greenspan, Ph.D.

Sande: That's a difficult question, because I don't really know. I think there has historically been here a certain degree of town-gown conflicts between the practicing physician, the academic physician, and the medical center. There certainly is competition between hospitals in San Francisco, a city that has too many hospital beds. There's always a battle for patients and for referrals.

I do think that because AIDS was not a disease that practicing physicians initially or even somewhat today felt comfortable dealing with, there was initially less competition for AIDS patients. Why didn't physicians feel comfortable dealing with AIDS? There have been a lot of theories. One of them is, that it's a brand-new disease with a lot of peculiarities that they were not trained to handle. So it was ignorance that was the first deterrent. There was a deterrent for a while, which I think is less obvious today, that the AIDS patient was dangerous to take care of because of the possibility of infection. And then there was the possibility that if they took many AIDS patients, they wouldn't acquire referrals of other patients because they didn't want to be associated with AIDS patients. I think that's markedly decreased.

But because of that, I think very early in the epidemic there was a cadre of young physicians, many of them our own trainees, and gay physicians, who were immediately thrown into the hopper to be the AIDS doctors, and then increasingly it spread out to many of the practicing internists and other physicians. This group, I think, cooperated very well. They all knew each other; they were friends. I think Donald Abrams did a wonderful job in developing the San Francisco County Community Consortium, which I think has sixty or seventy doctors in it. These are the people who take care of most of the AIDS patients. They have a monthly meeting; they have rounds; they do clinical studies together. They have been funded by a large grant from the NIH. So the disease certainly brought this group together, and they have worked wonderfully together.

Hughes: Had there been any precedent in San Francisco for close interaction between physicians in private practice and academic physicians?

Sande: Not that I know of.

Hughes: Were there tensions?

Sande: You know, I don't know that. You should talk to Don Abrams.[1] I'm sure that there's competition. One of the real problems has been that for a doctor who sees primarily AIDS patients, it's been suggested that if you get up to sixty or eighty AIDS patients in your practice, you go "psychotic." Because they're so demanding, require so much time, and are emotionally draining, you burn out. You need to spend so much time with them. And if they don't have insurance and are on Medi-Cal... Medi-Cal I remember at one time was paying something like thirteen dollars an office visit, which is probably 30 or 40 percent of overhead. So not only were the patients time-consuming, complicated, required a lot of energy and resources, there was essentially a negative incentive financially to care for them.

And yet, Bill Owen is one of these heroes who at great personal expense took on a large number of AIDS patients, and just worked with them, worked with them, worked with them.[2] I haven't been as close to that group as Donald would be. I've heard recently that the number of AIDS patients is decreasing for a lot of these practitioners, and that the epidemic is moving more towards the intravenous drug using population, which tends not to be as rewarding a patient population to care for.

AIDS Demographics

Hughes: Well, you said last time that the number of cases with AIDS is dropping. Did you mean overall, or in the gay population?

Sande: Well, in the middle-class gay population, it seems to be dropping. In the IV drug-using population, it tends to be staying the same, maybe a slight increase. And in the heterosexual population, particularly in the African-American, Hispanic group, increasing.

Hughes: The net effect is a decrease?

Sande: Probably flat right now.

Hughes: Is the change due to education?

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[1] See the oral history in this series with Donald I. Abrams, M.D.

[2] See the oral history with William F. Owen, Jr., M.D., in The AIDS Epidemic in San Francisco: The Response of Community Physicians (in process).

Sande: Well, no. I think I understand it. About 50 percent of the gay male population in San Francisco was infected before 1983, if the studies are correct, and I think they probably are. And there has not been a lot of transmission since 1982. So now that's thirteen, fourteen years, and the incubation period is about ten years. So half of them would be six to ten to ten and a half years after infection. So now, 60, 70 percent of them are developing symptoms, if they haven't died already. Now, that's the population that education clearly worked for, because transmission of AIDS dropped way down.

But since that time, the proportion of cases in the intravenous drug-abusing community, the crack-smoking community, has started drifting up, particularly in women. It's becoming more of a problem now than it was before. Ninety percent of our patients are still gay males, or gay males who are also intravenous drug users.

Early San Francisco AIDS Investigators

Hughes: You mentioned that the early AIDS investigators were by and large young people, in many cases beginning their careers, which was certainly the case with Volberding and Abrams and a number of other people. Why did Paul Volberding rise to the top of the heap?

Sande: I think Paul did very well, and I think his skills are communication and organization.

When you say AIDS investigator, you have to define what that means, because there are clinical investigators, of which certainly Paul has been very prominent, and you could name the other ones: it would be Margaret Fischl, Henry Masur, Doug Richmond, Marty Hirsch--I think that's the group. Then working with Paul, Donald Abrams did other things, Jim Kahn, Lorrie Kaplan, and more recently Mike Jacobson. John Mills was involved with AIDS for a while when he was here.

Clinical investigator as opposed to basic science investigator, and in that latter area, Jay Levy was one of the first. We recently recruited Warner Greene here [as head of the Gladstone Institute of Virology and Immunology], who is probably one of the best basic science investigators in AIDS in the world right now.

Paul was recruited to do something else [oncology], but I gave him complete flexibility to run with the AIDS thing, and supported him fully with resources and time and people. He also had an immediate patient population, and a very supportive administration, both at UC and the hospital [SFGH] and in the city. So I think he really fell into a wonderful situation, for which he was able to utilize his talents and skills of communication and organization. So I think it was a perfect mix for him in that setting.

Hughes: John Ziegler came here in 1981 with more of a reputation, because of research experience, than Paul Volberding had.[1] And then of course, there was Marcus Conant.

Sande: But Marcus was never trained as an investigator. Ziegler had developed a wonderful reputation in Uganda with the Burkitt's lymphoma program. But Ziegler wasn't here. Ziegler was at the VA.

Hughes: And that made a big difference?

Sande: Made a big difference, made an incredible difference, because the VA didn't have the resources, didn't have the AIDS population, didn't have the organization that we had.

Hughes: What made you think that this epidemic was going to be important?

Sande: There was never a conscious decision to say it was important. It just was there. It was there, and it was there in spades. We were opportunists. We said, "We've got to do something with this." It clicked. That's how you build a department; that's how you build an organization. But I don't think we ever sat down and craftily planned any of this. It was there to grab, and we grabbed it and ran with it. And the more we ran, the more success, the more accolades, and gee, after a while, we were on a roll. [laughs] Nobody was going to stop us.

Hughes: Have we said enough about who was making AIDS policy in San Francisco in these first four years of the epidemic?

Sande: Well, we talked about when Merv Silverman was head of the health department, the bathhouse issue. And we talked about the mayor's task force, which I think was very influential on all AIDS policy, once that became established. I think the health department here in San Francisco did a very good job in quelling hysterical fears and in charting a fairly rational course, and people followed.

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[1] See the oral history in this series with John L. Ziegler, M.D.

What's really interesting is that the things that the health department, the mayor, the mayor's task force, did in San Francisco led the world. I mean, everything emanated from San Francisco. We were always the first in everything, and everybody else sort of followed behind. It's a generality, but I think it's very, very true.

We could see that when we went elsewhere. I used to run the Infectious Disease Society of America [IDSA] symposium on AIDS. Most of the people we got to talk were from here, on almost all the issues. San Francisco has been very, very powerful, influential.

AIDS Activities at San Francisco General

Hughes: As AIDS activities expanded at San Francisco General, was there any resistance from other hospital services to what must have been a drain on staff and finances?

Sande: I think the finances actually were increased because of AIDS.

Hughes: In general?

Sande: Yes. We attracted political attention and as a result attracted resources. I'm sure there were some jealousies, and probably some concerns that we were getting too much publicity. There's a lot of other good things at San Francisco General. I guess one of the things we were reacting to was, for years the trauma service was held up as the most visible part of the organization, and we (in medicine) were sort of proud to have something of our own [AIDS activities] that matched them for visibility. And pretty soon, all the divisions of medicine were somehow involved in AIDS, and also the other departments--certainly OB/GYN, pediatrics, ophthalmology, psychiatry, and surgery.

I think one of the real heroes of the AIDS epidemic is Bill Schecter, who is our chief of surgery. Bill Schecter, working with Julie Gerberding, really did a lot to quell the fears of surgeons operating on AIDS patients. Bill was always a very, very articulate presence, scholarly presence in the surgical world on responsibility of surgeons to care for AIDS patients, and took a passionate look at the data relative to risks, innovative ways for reducing risks, i.e., double-gloving. He really is a wonderful guy, and a wonderful speaker. He did a lot to quell the hysteria that Lorraine Day had whipped up.

And before Bill, Frank Lewis was also very good. Actually, most of his time Frank Lewis was head of surgery, and he was also a very strong believer in the rational approach and a surgeon's responsibility to operate. Both those guys did a great job. So it wasn't just the AIDS division in medicine that was doing this.

The Multidisciplinary Approach

Hughes: A multidisciplinary approach to a disease is not unique to AIDS, but is the wide spectrum of the specialties focused on one disease something new?

Sande: Sure. Not focused, but a part of. See, the specialties all had their own arenas, and AIDS was a small part of most of those arenas for the other services. But it was a vital part, and they certainly participated in it.

Hughes: Can you think of any disease that called upon such a diverse approach?

Sande: Trauma.

Hughes: But not another infectious disease.

Sande: No.

Hughes: So of course, that forced cooperation and collaboration, didn't it? Because of the very nature of the disease itself, one specialty couldn't cover it adequately.

Sande: Right.

Hughes: So the disease itself--

Sande: Was a unifying force.

Hughes: Interesting. Were there non-San Francisco General physicians seeing AIDS patients here at the hospital?

Sande: Yes, people in private practice who have clinical appointments come and work in the AIDS Clinic. There were a number of those. Steve Follansbee, who has a big practice in town.[1] Mike McCune,

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[1] See the oral history series in the AIDS community physicians series with Stephen E. Follansbee, M.D.

who is the inventor of the SCID [severe combined immunodeficiency] mouse model, is a very, very prominent scientist worldwide, comes up every Monday morning and sees patients in the clinic. Yes, there's a lot of volunteer help that still goes on.

Hughes: Does a private practitioner lose his patient when he is admitted to SFGH?

Sande: Most private practitioners admit their patients to their own hospitals.

Hughes: Even when the best treatment for AIDS is here?

Sande: I don't know the answer to that. I think there were some patients admitted here who would go back to their private practitioner, but usually they were admitted to the private hospital. But a lot of those private practitioners were also working in the AIDS Clinic. So there was some connection. If the patient was admitted SFGH, it probably was the result of their private physician's relationship with the AIDS program at SFGH.

In terms of best care, that's a tough one. I'm not sure there's a best care. Certainly this was really good care.

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Sande: Patients elsewhere didn't have as much access to the clinical trials and the new drugs as they did here. But I would be very careful not to say that other hospitals didn't provide good care.

Hughes: When I asked that question, I was thinking in a broader sense than just the medical. I was thinking of what we had talked about last time--

Sande: Access to the resources, access to the community placement, and things like that.

Hughes: Right, and the atmosphere of the inpatient ward.

Sande: That was a real plus. That's what we had to sell. That also helped to attract a lot of private patients to San Francisco General.

Projecting the Need for Hospital Beds for AIDS

Hughes: I understand that one of the responsibilities of the mayor's advisory committee was to try to project future need for AIDS beds.[1] How did you go about that?

Sande: Well, it was two-fold. One of my agendas, which I didn't speak about a lot, but I did speak about occasionally, was that I was adamantly opposed to making San Francisco General an AIDS hospital. We have here probably the best, if not the best, one of the real top training programs in internal medicine in the country. It's a training program that includes the VA, Moffitt Hospital, and SFGH. I was concerned when we saw this tremendous onslaught of AIDS patients that the AIDS population would crowd out everything else, and that our teaching program would suffer. There would be very good caring for AIDS patients, but trainees would lose a lot of the other important aspects of the training.

So one of my agendas was to be sure we never got more than a third of our medical patient population in AIDS. We had made potential arrangements once it got to that point to divert patients to other hospitals. We would still maintain some care of those patients, but we would unload the patients if it came to that point.

Hughes: So you had essentially a quota.

Sande: It never went into effect, because the market forces and the expertise of others started to take over, and if anything now, we can take more AIDS patients. So it never became a problem, but I was very concerned about that.

Now, in terms of projecting hospital beds and how many were going to be needed, that's where Phil Lee, who was a very important part of the mayor's advisory task force, and the people that worked with him, and Ann Sikowsky from Palo Alto, and some of the health planners, were helpful in looking at the data, as was Andrew Moss. But there was a lot of guessing, although there were mathematical modeling that could project that.

Hughes: Was the projection fairly accurate, as it turned out?

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[1] See for example, Meeting Minutes, Mayor's Advisory Committee on AIDS, October 22, 1984. (AIDS History Project Archives, Special collections, UCSF Library, Ward 86 papers, carton 1, folder: to PV [Paul Volberding] Oct.-Dec. '84.)

Sande: It was for a while. The increases were certainly projected, and the increases were seen. Yes, I guess it was pretty accurate. But then also other factors were at work, such as increasingly we were able to make diagnoses and initiate therapy in the outpatient arena, which didn't require a hospital bed. We reduced our length of hospital stay.

The other thing, by the way, that was very important to the training program and to the hospital is that our length of stay got down to around seven days, where in New York it was fifty days.

Hughes: I saw some figures for 1986 for the considerably lower cost for the average care of an AIDS patient in San Francisco, as compared to elsewhere, and it was something like $29,000 per patient.

Sande: Yes, and a lot of that was Ann Sikowsky's data.

Hughes: Was the lower cost largely based on shorter hospital stay?

Sande: Yes. It was the San Francisco model: treat the patient at home, in the community.

Hughes: Well, I saw in the minutes of a meeting of the mayor's advisory committee of November 5, 1984 that twenty to twenty-three patients could be accommodated in 5A.[1]

Sande: We started with 5B in July '83, and then expanded from twelve patients to twenty to twenty-two patients.

Hughes: Anyway, the mayor's advisory committee projected 150 AIDS cases per day needing hospitalization in San Francisco by the summer of 1985.

Sande: That's probably about right, because we always had about a third of them.

Hughes: That number didn't worry you?

Sande: I didn't want them all to come to San Francisco General, for strictly personal purposes relative to the training program. Kaiser [Permanente Medical Care Program] was real good with AIDS; they always had about a third of the patients, too. They were second behind us.

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[1] Minutes, Mayor's Advisory Committee on AIDS, November 5, 1984. (AIDS Resource Program Archives, UCSF, AR92-20, carton 2, folder: Mayor's Task Force on AIDS.)

Hughes: Aren't you being overly complimentary? They didn't have a choice if somebody had Kaiser coverage, right?

Sande: No. I'm being positive about their response, because they didn't shrink from taking them. They developed good patient care activities. George Matula over at Kaiser in San Francisco became a real leader in the area. They were proactive. You didn't get the sense that Kaiser was trying to shirk its responsibility at all. At least, that was my perception.

Hughes: So that 150 cases, which is considerably over the twenty-three maximum that the General felt it could accommodate on 5A--

Sande: Well, no, we never really said twenty-three maximum. We usually probably had thirty to forty.

Hughes: But scattered around the hospital.

Sande: Scattered, yes, and the twenty-three on the AIDS ward.

Hughes: Okay, even if you took forty, you still had 110 patients that you had to hospitalize elsewhere. Was the committee pretty sure that it could find beds elsewhere?

Sande: We were worried about it. That's when I was very concerned about us becoming an AIDS hospital.

UCSF Task Force on AIDS and Mayor's Advisory Committee on AIDS

[Interview 3: January 3, 1994] ##

Formation of the Mayor's Advisory Committee

Hughes: Dr. Sande, could you talk about the interrelationship of the UCSF Task Force on AIDS and the Mayor's Advisory Committee on AIDS?

Sande: Okay. The UCSF Task Force on AIDS was the committee appointed [in March 1983] by Julie [Julius] Krevans, who was then dean, to deal with infection control. The group was large and included members of the health department, including Merv Silverman, and members of the hospital; Geoff Lang was the SFGH administrator at that time. This in '83 and '84 was the group at the health department and in the hospitals that talked about AIDS.

We then gradually merged into a consulting body for Mayor Feinstein. They were the same players, and we then formed what was called a mayor's advisory committee on AIDS, that I suspect started in the fall of 1984.

Hughes: Do you remember what the impetus was?

Sande: As I remember, at this time there had been a long, drawn-out process and a group of people independent of this body that was dealing with the bathhouse closure issue. I recall numerous evening meetings would go far into the night discussing that issue. Paul Volberding and I were on it; Merv Silverman was reporting to the mayor. I think the mayor realized that she would benefit from a more structured organization whose purpose was to keep her informed and advise her on the extent of the epidemic, the direction of the epidemic, new problems of the epidemic, political responses to the epidemic, political statements that needed to be made about the epidemic.

So while a small group of us were meeting with Merv Silverman to talk about closing the bathhouses, this large group of the UCSF AIDS Task Force, which included health department officials, sort of became, or many members of this group became, the mayor's advisory board.

Hughes: She officially appointed you to that committee?

Sande: She appointed me, and she would make recommendations about who should be on it, and then I would essentially invite whomever I wanted. What was neat about it is that we would bring her up to date about not only issues in the city and the state, but also around the world. We had people visiting who were up to date on this because they were the people doing the research, and finally Nathan Clumeck, when he first described AIDS in Africa. And they all met with Feinstein. As they came to town, we would bring them to see the mayor, and she would open her arms to them, because she was the mayor who knew more about AIDS than any other mayor in the country at that time. That would have been '84 to '88 [January 17, 1988].[1]

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[1] Information courtesy of Sally Osaki, Office of the Executive Assistant to the Director of Health, San Francisco Department of Public Health.

Advising the Mayor

Sande: During the last months of her tenure, we were meeting with her almost once a month. She had this insatiable thirst for information about the epidemic.

Hughes: Which might or might not be specifically applicable to San Francisco?

Sande: It was much broader than San Francisco.

Hughes: Yes, if she was interested in Africa, it must have been.

Sande: I think I said this last time: It was a wonderful way for a politician to use her academic resources to educate herself and help decide policy. I think that's without precedent. And boy, if I were running a city or a state or a country, I would really have this independent body with no political aspiration, nobody vying for attention. In fact, all this stuff was secret. We never mentioned a word about it to the press or anybody else, because we only had one agenda, and that was to educate her. She appreciated it, and she respected it, and we did too. It was a remarkably nonpolitical body.

But when Silverman finally decided to close the bathhouses in the early fall of 1984,[1] then Feinstein became obsessed with the delay, delay, delay, and felt he should have made a stronger statement earlier. Then I was appointed, because of this body [UCSF Task Force on AIDS], to chair her advisory committee.

Hughes: You mean because you were chairman of the UCSF Task Force on AIDS?

Sande: It naturally followed, because the same people became part of her group. Now, she added a few others, like Jim Foster, who was on the board of the health commission. He was a gay man who actually died of AIDS a number of years ago. Phil Lee, who became head of the city's health committee [San Francisco Health Commission], joined; we appointed him. And then when Silverman was replaced by Werdegar as health department director [1984], David Werdegar became a member of that committee. Actually, I think he was a little threatened by it, because it was a direct link to the mayor on health that didn't go through the health director, so there was a natural potential for conflict. We actually worked it out

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[1] Silverman closed the bathhouses and private sex clubs in San Francisco on October 9, 1984.

fairly well. I was sensitive to that potential conflict, and he was sensitive to what we were trying to do.

Hughes: You said a few minutes ago that you had leeway in appointing people to the committee. Now, did you really mean that, or did you mean that you invited speakers on specific topics?

Sande: As I remember it, I also appointed people. I think I appointed Julie Gerberding. I think I appointed Connie Wofsy. Paul Volberding was always part of it. I think I appointed Andrew Moss to be part of that. I'm not sure how the dynamics worked, but it was a heterogenous group, and I think the mayor appointed some and I appointed some.

Hughes: Where did the group meet?

Sande: In the mayor's office. We discussed many issues. We were very concerned about who would care for the growing numbers of AIDS patients, how they would be cared for. This was a time when there was a tremendous stigma and fear of the private hospitals being branded AIDS hospitals. Besides, it was a new disease, and people didn't understand it, didn't know how to care for it, so there was a lot of uncertainty. So we were concerned about where people with AIDS were going to be taken care of, where they were going to be hospitalized, really concerned about who was going to pay for it, because the reimbursement was not very good for this disease, and a lot of these people required governmental support.

So we would meet, look at the data, and we would always have an update at these meetings by whoever the AIDS epidemiologist was. Dean Echenberg, and then George Rutherford of the health department's Bureau of Infectious Disease Control would update us on the number of cases that month or the month before, trends, new things. And then we would crystalize, distill all the information, look at the national scene, look at the international scene, and then we would have a program to present to the mayor.

Hughes: It makes sense to you that the committee was organized as late as fall of 1984?

Sande: This part of it did. I think we had met with the mayor several times before when Silverman was chair of the committee. You see, when he was the driving force as head of the health department at the same time he was trying to close the bathhouses, we would meet with the mayor to give her updates on this process. I would give her updates on what was happening at the UCSF meetings about infection control and risk to health care workers, which was always a big, big concern.

And then when Silverman fell from favor, she put me in as the chairman of the committee, and then we started having these other meetings to talk about preparation. But our group continued until the very last day of her tenure in office, and meetings increased in frequency as she reached the end of her term.

Mayors Art Agnos and Frank Jordan

Hughes: And then died with--

Sande: Agnos. He didn't want anything to do with us.

Hughes: Why was that?

Sande: I don't know. We met with him twice, offered our services, and didn't hear from him again.

I met with [Mayor] Frank Jordan and said, "We had this really positive body of knowledgeable people whose only job was to keep the mayor informed on what was happening." I said we would be more than happy, I'm sure, if he was interested, to do it again. He said, "Oh, well, of course," and he never did it.

Recognizing AIDS as a Sexually Transmitted Viral Disease

Hughes: Moss says in his oral history that he put data on the board at what he called the Mayor's Advisory Committee on AIDS.[1] He didn't give a date, but I suspect it might have been 1983, because he was working from his census tract study. His point was that he had to convince you, the group, that AIDS was a sexually transmitted disease. He maintains in the oral history that it was his data that convinced you that it was a sexually transmitted disease. You couldn't have been doubting that as late as fall of 1984 after the discovery of the virus.

Sande: I remember Andrew being particularly prophetic about intravenous drug use, and it's the second demographic wave of the epidemic. I don't specifically remember him trying to convince us that it was

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[1] See the oral history in this series with Andrew R. Moss, session 1, September 30, 1992.

a sexually transmitted disease, but that wouldn't be surprising that I wouldn't remember that point.

Hughes: Do you remember ever having doubts about that?

Sande: No, I don't remember having doubts about it. I certainly had doubts about where the virus was, or how it was transmitted sexually. But once it was occurring in just gay males, it had to be a sexually transmitted disease. But why it was particularly gay males, we didn't know.

Hughes: And it had to be a virus?

Sande: That was the most logical thing. Everybody thought it was probably a virus.

Stigma

Hughes: At the first official meeting of this mayor's advisory committee in October of '84, you introduced the idea of equitable distribution of AIDS patients.[1] Do you remember how the committee set about to try to allocate AIDS cases throughout the city?

Sande: As I said before, nobody was anxious to jump in and care for patients. I shouldn't say nobody, but there was a general sense that the private hospitals would look very bad if they were known as an AIDS hospital. At that time, there was a concern that these individuals were infectious to other people. So the hospitals were concerned that if they had AIDS patients, other patients wouldn't want to come there. They were concerned that if they had AIDS patients, that they wouldn't be able to recruit good housestaff to their programs.

Hughes: What about homophobia?

Sande: I always thought that was over-sensationalized. I didn't have a good understanding of homophobia. I didn't think that any hospital in San Francisco would be penalized, or a physician would be penalized, for taking care of homosexual males. I didn't feel doctors had an aversion to taking care of homosexual patients. I thought it was much more the fear of infection and fear of the

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[1] Minutes, Mayor's Advisory Committee on AIDS, November 5, 1984. (AIDS Resource Program Archives, Ward 5A, SFGH, carton 2, folder: Mayor's Task Force on AIDS.)

unknown. Now, this has been studied and written about a lot--maybe that fear brought out homophobic responses in people.

But I always thought there was more of an aversion to intravenous drug users, because of their crime-associated behavior, than there ever was for gay males. Now, I know a lot of gay physicians and gay people don't think that's true, but I didn't think homophobia was a big problem, particularly in San Francisco.

Hughes: I think San Francisco is a special case, but to this day there are people who consider homosexuality a crime, at least a crime against nature, and in some states it is a crime.

Sande: Oh, yes. I'm only talking about San Francisco. I'm not talking about outside the San Francisco area. I bet it was '83, I made a tour through the Bible Belt, and lectured in Spartansburg, South Carolina, where Bob Jones University is. There were some places that were really totally homophobic.

Hughes: You were lecturing on AIDS?

Sande: Yes. And the response was, "Good God, God's finally awakened and found a way to get rid of these people." But of course, I didn't find it at San Francisco General, and I certainly didn't find it at UCSF, and I didn't find it in the city. But the fear of contagion and the fear of the unknown I think was a definite fear and a realistic fear. That's why we felt that if every hospital took AIDS patients, the stigma would be neutralized. And I think that's what eventually happened. I don't think it was anything we did. I think it just happened.

Hughes: Because it became known that AIDS could not be transmitted casually? That there was not a great danger of infection? Was it as simple as that?

Sande: I think that may have helped, but I think it was happening regardless. Hospital boards were afraid, but it turned out that the decision to admit or not admit AIDS patients isn't controlled by hospital boards or hospital administrators; it's controlled by the physicians. So through the medical society and through the educational programs that we all put on, physicians assumed their natural Hippocratic responsibility to care for all patients. So all the hospitals eventually had AIDS patients. But I don't think it was anything we did politically, or did using the mayor's office, to make that happen. I think it just happened. And certainly, once it looked like AIDS was not disseminated by casual contagion, that helped an awful lot in easing the fears of the health care workers.

Hughes: What about easing your fear of San Francisco General becoming labeled as an AIDS hospital?

Sande: We were not concerned about our patient population, because we're the hospital of last resort. We don't have a lot of private patients. So we were never concerned that if we had lots of AIDS patients, other patients wouldn't come here, because they come here anyway. We were concerned that it would destroy the training programs, that if we became nothing but an AIDS hospital, then where do you learn about diabetes, and where do you learn about heart disease and other things? That was one of my personal and selfish concerns, and it's reflected in that document in '83 and '84, describing the hospital's response.[1] We actually got the mayor to propose that we could cut off the number of AIDS patients at San Francisco General and distribute them if we had to. We never had to, but we worked hard to get that feeling that we would not just let San Francisco General become an AIDS hospital.

Hughes: There was talk in that same set of minutes about generating a list of physicians throughout the city who maintained that they would be willing to treat AIDS patients.

Sande: Yes. There was a concern that initially physicians wouldn't do it. Today, a small group of physicians see the vast majority of the AIDS patients. But I don't think that it any more is fear of contagion. I don't think it's homophobia. I think it's just that the disease has become complicated, and certain internists, infectious disease specialists, oncologists, and some family practitioners who have mastered the art and have kept up with the changing scene of AIDS are the ones who do most of the work. Which is not unusual, and it has no negative connotation.

Consultant on AIDS to the San Francisco Medical Society, 1985-Present

Hughes: You said off-tape that you didn't play much of a role as a consultant to the AIDS task force of the San Francisco Medical Society. But another thing I learned from those minutes was that the mayor's advisory committee decided that the society would be the one which sought the list of physicians.

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[1] Sande, Merle A., "The AIDS epidemic: Blueprint of a hospital's response." Transactions of the American Clinical and Climatological Association, 1987:99.

Sande: Yes. The president of the medical society was also on our UCSF task force, and then on the mayor's advisory body.

Hughes: [Glenn] Molyneaux?

Sande: Yes. He was a very loyal member of that group who came to all the meetings and was very supportive. A wonderful, wonderful human being.

Hughes: Did the society indeed help to solicit AIDS physicians?

Sande: I don't remember how far that went, or if it was ever really necessary to do it. But there was an active process of engaging physicians to the need for it, and as I remember, it was a pretty positive response.

I do think it's important that we get Sally Osaki, if she has minutes of those meetings, to make them available to us.[1]

Obtaining Funds from the State of California, 1983

Hughes: The UC Systemwide Task Force on AIDS, as I understand it, was fallout from the money that came from the state of California through [Assembly Speaker] Willie Brown, for AIDS research.

Sande: Right. In '81, Mike Gottlieb from UCLA reported five cases of Pneumocystis pneumonia in gay males.[2] Shortly thereafter, we started seeing--Marcus Conant was one of the first ones here in San Francisco who started seeing Kaposi's sarcoma in homosexual males. Then we started seeing here at San Francisco General a number of homosexual males with strange diseases, with toxoplasmosis, cryptococcal meningitis, toxoplasmic encephalitis, Pneumocystis, Kaposi's sarcoma, et cetera.

So stimulated by this explosion of bizarre findings, a group of our investigators, which included Marcus Conant and Jay Levy, I think John Ziegler, maybe Paul Volberding, and a number from UCLA

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[1] Sally Osaki, now retired as Executive Assistant to the Director of Health, was approached in March 1994 but did not possess minutes. However, she graciously supplied copies of various documents relating to ex-Mayor Dianne Feinstein's AIDS activities.

[2] M. Gottlieb. Pneumocystis pneumonia--Los Angeles. Morbidity and Mortality Weekly Report, June 5, 1981, 30:250-252.

--Mike Gottlieb was the leader of that group, and I think it included Ron Mitsuyasu and a few other people--met with Willie Brown at the airport in Los Angeles and said, "This epidemic is scary, we need money." Willie answered, "How much?" They said, "Jeez, we hadn't thought of that." So they came up with maybe a million or something, and he said, "I'll give you two," and it ended up with being $1.9 million, if I remember correctly.

Hughes: $2.9 million, I think.[1]

Sande: Was it? Could be.

Anyway, so Willie went back and got a bill passed in the legislature--yes, I guess it was $2.9, because it was $3.1 the next year; I remember that. So that's all fine and good, but the state of California is not really a granting agency for medical research. So now you have money to give, who do you give it to and how do you decide who to give it to, because immediately you're going to have a lot of people who want it.

The Universitywide Task Force on AIDS

Formation

Sande: So they gave it to the University of California, systemwide, as a line item in the UC budget. The university said, "Well, we're not a granting agency. What are we going to do with this money?" So [UC President] David Gardner, at the suggestion of Julie Krevans, who was chancellor then, appointed a task force, and I was the chairman.

Hughes: Why?

Sande: Why? I was in a position of responsibility in the UC system as head of the Department of Medicine at this hospital, and I was an infectious disease specialist. Those are probably the reasons why. I certainly had done nothing to build a reputation that had anything to do with what we were talking about, although I was leading the UC effort on AIDS. See, the UCSF Task Force on AIDS was started before the systemwide task force, and I was the chairman of that. Krevans, because I was an infectious diseases specialist, had appointed me to that, so then I'm sure he

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[1] Shilts, p. 281.

influenced Gardner to appoint me to the other committee. I imagine that's what happened.

It was a small group. The first meeting included Mike Bishop, who immediately resigned, because he saw it as a political body, not a scientific body. Ira Goldstein took his place.

Hughes: Is that typical of Bishop?

Sande: I don't know. I think Mike saw it as perhaps not a way he wanted to spend his time.

Then Larry Freedman [M.D.] from UCLA who was head of medicine at Wadsworth, VA; Jack Stevens [D.V.M., Ph.D.], who was chairman of microbiology at UCLA--he's a vet, a wonderful guy--; Abe Braude [M.D.], who was head of infectious disease at University of California San Diego; Tom Cesario [M.D.], who is now chairman of medicine at UC Irvine but was then head of infectious diseases; and Bob Cardiff [M.D.], who was a pathologist at UC Davis; and then Dr. Reeves--

Hughes: William.

Sande: Bill Reeves [Ph.D.], yes, who was from Berkeley, an old virologist who worked on mosquitoes.

Hughes: Encephalitis.[1]

Sande: Yes. So that was our group.

Hughes: Do you know why those particular people were chosen?

Sande: Because they all had interest in infectious diseases and viruses. So they felt like they would be able to identify good science.

So we met, and then Bishop resigned, and we appointed Goldstein as the other member from UCSF other than myself. So we had two from UCLA, two from UCSF, and one from the other schools.

Hughes: Was this money to go just to UC campuses?

Sande: Originally, it did, because it came to UC. Then after the first session, we said, "Well, this isn't fair." Actually we never got

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[1] William C. Reeves, Abrovirologist and Professor, UC Berkeley School of Health, an oral history conducted in 1990 and 1991 by Sally Smith Hughes, Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 1993.

credit for this. This is the most amazing, frustrating thing. We as a group decided that the RFA [Request for Application] should go out to the other campuses, and specifically to the medical schools at USC [University of Southern California] and Stanford, but also Cal Tech, I think.

Hughes: Regardless of whether they were doing AIDS research or not?

Sande: Well, no. All of this money was to go to AIDS research. This was wonderful money, because it was used to stimulate bright young people to think about this new disease.

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Sande: So it was used to entice people into looking at the problem, good, young scientists. And it worked; it really worked.

So we then decided to open this up to other campuses, and recommended to the president to let us do this. The UC administrator here was Cornelius L. Hopper, from systemwide, a very nice person who I got to be very good friends with. Well, the next year when we went to the legislature and made our report --let me see. The first time I went [1984], I reported on our progress to Willie Brown in Willie Brown's office with [State Assemblyman] John Vasconcellos, [Senator] Dave Roberti, [State Assemblyman Tom] Campbell, and [Assemblyman] Art Torres.

Senator Roberti's from Hollywood, John Vasconcellos is chairman of the [California] Assembly Ways and Means Committee and from Santa Clara, Art Torres is from L.A., and Willie is from here. I'm not sure if [State Assemblyman William] Filante was there or not. Anyway, I made this report, and they criticized it.

But then I got in front of the Assembly Ways and Means Committee, I guess, and Torres lit into me because we kept all the money at UC. Why were we so stingy and self-serving that we would just give the money to ourselves? And I said, "Well, Senator, we have just recommended to the UC president that we open this up as a statewide competition among all the universities." And he said, "That's a bunch of baloney. We know you're not doing it."

Anyway, we never got credit for doing it on our own. But he accused us of only doing it after political pressure was brought to bear, and that's not correct. But that's the way that it was written. I got very angry and very flustered at that, my inability to make him see, but he was a real politician. He was staging this, I guess. Phil Lee said I behaved very badly at that meeting. [laughs]

Hughes: Because you showed your temper?

Sande: Yes.

Delay in Fund Distribution

Hughes: But there was controversy even before that, I believe. Randy Shilts wrote about the delay, as he and apparently others saw it, in the distribution of those Willie Brown funds.[1] The bill was passed in July [1983], and I think the task force first met in October.

Sande: And we had money going out the next spring. That's the natural reaction of reporters--it seems so simple to give money away. It's very difficult to give money away and to be accountable for the way you decide and how much you give. We thought it was very important that it was not a political process, but it was a scientific process. Well, we had money available, and then we had to send out the announcement; we had to say what it was for; we had to develop a form; we had to develop a study section to review the grants when they came in; we had to have a way of deciding priority scores and who the money should be awarded to and who it shouldn't.

The criticism came because of course the people who met with Willie Brown thought they should get the money. But we couldn't give them the money. That would have been absolutely untenable. They had to show that they deserved the money, and there had to be a competition.

Hughes: Would it have made any difference if these had been really senior people?

Sande: No. They still wouldn't have gotten it. UC was given the responsibility of being sure this money was spent as well as possible. It was remarkably speedy. It was the most rapid process I've ever been associated with, in terms of putting an organization together, getting out requests for grants, getting the grants in, reading them, evaluating them outside the political system, and then awarding them. That that should happen within eight months was absolutely remarkable, as far as I'm concerned.

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[1] Randy Shilts, "University Assailed for Delay on AIDS Funds." San Francisco Chronicle, August 25, 1983, p. A10; Randy Shilts, And the Band Played On, pp.357-358.

Hughes: The Chronicle quoted Rudi Schmid as saying that the delays and the university administration's review of requirements were "totally unacceptable" and "ludicrous".[1]

Sande: [laughs] Good for Rudi.

Hughes: The article is dated August 25, 1983--before the task force had met.

Sande: Well, I think the process was a very good one. We actually were very proud of that process, because it worked very quickly and has been remarkably free from political influence. What turned Mike [Bishop] off I think was he felt like his time was going to be totally wasted, and that political pressure would be very strong to award the politically astute investigators, and it never was.

Hughes: Did you feel any pressure from Sacramento?

Sande: I didn't. I don't work for them. I'm not dependent upon them. I think David Gardner did, and I think UC did.

Hughes: How was that expressed?

Sande: Well, the legislature determines the university's budget.

Hughes: Be a little more specific. What would Sacramento have had Gardner do?

Sande: There were examples where investigators didn't get funded, and they would go to their legislator, and the legislator would investigate why, when people are dying of AIDS, didn't we take every bright idea and fund it. Then if you don't, we'll certainly be sure that the university's budget is affected by this. Rumors were perpetuated. The legislature enjoyed looking at distribution of grants--who was getting the grants, why weren't more grants going to Stanford. Actually, that's where I got in trouble, because when we did open it up, we opened it up late, and Stanford and USC investigators didn't have very much time to respond to it. As a result, their grants were not very good, and they didn't get what some thought was their fair share.

What we tried to point out is that there wasn't such a thing as a "fair share." It was based upon the quality of the grant application, bringing in outside reviewers from around the country

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[1] Randy Shilts, "UC assailed for delay on AIDS funds." San Francisco Chronicle, August 25, 1983, p.A10.

to review these grants. We had no influence on them ourselves, because we got other people to review the grants.

Hughes: Leaders in AIDS research were doing the reviews?

Sande: Yes.

Hughes: Was it like an NIH study section?

Sande: It was a study section, and it grew increasingly large and complex as some more money came in. I'll bet it's up to $100 million now that the group has given out. I was chairman for five years [1983-1988]. We put a process into place that I think stood up very well under political scrutiny. I think that there were people who were very mad that we just didn't give a lot of money to certain people who had helped get the money in the first place, and there will always be some sour grapes over that. But I think the process worked very well in terms of getting quality science.

Facilitating AIDS Research

Hughes: I saw a letter written in January 1985, which was signed by you and Robert Cardiff, announcing Jay Levy's virus, and the fact that it was available to researchers. It struck me as an unusual thing for a committee to do, which I thought was strictly a funds-distributing unit.

Sande: Our job was to facilitate research on AIDS, any way we could. So we did a couple of very creative things. First of all, we created tissue banks--John Greenspan runs the one up here at UCSF. There was one down south at UCLA. We created a central laboratory for routine assays at Davis, and first of all, it was just the ELISAs [enzyme-linked immunosorbent assays] for HIV. Then it was more and more sophisticated assays.

Hughes: Where was the central lab?

Sande: Jim Carlson ran it at UC Davis.

Actually, the task force had complete power. We didn't have to answer to anybody. In the charter or in the law we had to report to the Assembly Ways and Means Committee once a year or something. So we created a tissue bank, created a central laboratory with Carlson, finally got tremendous fights from southern California, so we created another lab down there. Then, we funded two centers, one at UCSF and one at UCLA. We gave

blocks of money to these centers to create small grants, local interest in studying HIV--clinical, basic, whatever.

Hughes: Now, those are the AIDS clinical research centers?

Sande: Yes.

I think our most successful investment was developing a consortium in southern California that [John A.] McCutchan ran from San Diego, and it included San Diego, Irvine, USC, and Stanford. This group of four institutions had been incredibly productive in doing clinical trials of treatments of AIDS-related conditions. Unbelievably successful.

Hughes: In what sense?

Sande: Well, they were the first ones to demonstrate that we should use steroids for Pneumocystis pneumonia. They were the first ones to test trim [ethoprim] sulfa versus pentamidine and show trim sulfa was better for prophylaxis--a whole series of very important observations done with the state money that beat any of the ACTG [AIDS Clinical Trial Group] or national investments of much more money. This was a very creative thing.

And then we made reagents available, one of which was Jay Levy's virus, because Jay was heavily funded by this task force--never enough, according to Jay.

Hughes: Was it a significant advantage to have a local virus, so to speak?

Sande: I think it was used. All of these things were significant advantages, I think. The central lab, the tissue banks were extremely effective. People were encouraged to share, and basically they did. Some didn't, but most did. There had been a real problem with Bob Gallo in sharing. That's why we didn't want to have to face that issue. I actually think we put it in the RFP that your reagents, after given proper identification and acknowledgement, could be used by other investigators who were funded by the statewide task force.

Hughes: But not others?

Sande: Priority was given to funded investigators.

Hughes: My understanding is that by being reluctant to share, Gallo diverted from the code, that this sharing of reagents and

organisms was considered part of the etiquette of science, long before the AIDS epidemic.[1]

Sande: Not necessarily. There's no etiquette in science, I don't think. Basically people are pretty good people, and if you're in it to push back the frontiers of science, you certainly will share.

Hughes: There was no code that said scientists should share? I don't mean a written code necessarily, just an understanding among scientists that you shared.

Sande: I'm not sure.

Hughes: The reason I think that there must have been some sort of understanding is that Crewdson, the Chicago Tribune journalist who did an exposé of Gallo, contended that Gallo required a form to be signed before the virus was released from the laboratory. In fact, in the case of Jay Levy, he just didn't release it, and Don Francis had trouble obtaining an NIH virus.[2]

Sande: That's probably hyperbole. What would Francis have done with the virus anyway?

Hughes: Well, he was working on it.

Sande: He's not a bench scientist.

Hughes: He had been collaborating with the Pasteur Institute.

Sande: But he was an epidemiologist.

Hughes: Yes, but he was also a virologist. He has a D.Sc. in virology. He worked with Max Essex at Harvard, so he did have some virological background. One of the things amongst many that CDC was doing was working on the isolation of the virus.

Sande: Well, among good people, people usually share. But this gave us an opportunity to make it an official thing. And in general, it worked out very well.

By the way, the other thing that the task force did that was creative was every year we had a meeting, and had the research

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[1] John Crewdson, "The great AIDS quest." Chicago Tribune, November 19, 1989, section 5, p.9.

[2] Crewdson, p. 9; also see the oral histories in this series with Donald P. Francis and Jay A. Levy.

presented. It was really a neat club that was developed to present the science, to have long discussions, to talk about what was going on. I thought that was also a big plus. So we solidified and enticed people into studying HIV in California, with the money, with the science, with the fraternity, the camaraderie that developed, the sharing of ideas, the sharing of reagents. And I think it really worked; it really did.

Hughes: So the annual meeting was a forum for explaining, describing, what research the state money had supported?

Sande: In a way. But see, nobody else was doing this. Nobody in the country was doing this. We were already having meetings, showing that many observations had been made during the last year. So that went very well. It went very fast. It was way ahead of the federal government.

Political Clout

Hughes: It seems to me that you were in a position of considerable power as chairman of the systemwide committee, an advisor to the mayor, and also head of the UCSF Task Force on AIDS. Did these positions give you political clout?

Sande: I don't know. I certainly think that we had a direct line to plead our case for resources for AIDS care at San Francisco General. And Feinstein was always quite supportive of our needs to care for AIDS patients. So if political clout is reflected in terms of resource distribution, I'm sure that did help us. But in terms of personal power, I don't really know what that means in this sort of arena. Visibility. We certainly became very famous. But I'm not sure fame has been followed by fortune. [laughter] We're still here, we're still doing the same thing we were doing before. None of us ever tried to use it for political advancement in any way, shape, or form. I don't think that was ever our agendas.

Gladstone Institute of Virology and Immunology, San Francisco General Hospital

Sande: We became very visible nationally. I became president last year [1992] of the Infectious Disease Society of America, and certainly

have had a big influence, I think, on the political process in AIDS nationally and internationally.

I guess the one place where my being at a certain place as chairman of the statewide task force may have influenced something is when we got the Gladstone building. In a casual conversation with John Vasconcellos we said, "In looking at how you really approach a complex problem like HIV, if you get a group of highly talented, brilliant young scientists who are working in the same arena, working on the same area, there is synergy between scientists. So what would make a lot of sense would be to have an institute basically focused on AIDS research."

At that time, Vasconcellos was chairman of the Assembly Ways and Means Committee. I was actually chairman of a subcommittee on research of the Assembly Ways and Means Committee; there was a small group of us. So I proposed that what they should do is build a building for basic AIDS research. That's what was needed. And then I half-kiddingly said, "And I think San Francisco General would be a great place to have that."

Well, Vasconcellos said that was a big joke, but he would put it on his wish list. That year he had, I think, twenty-one things that came out of the Assembly Ways and Means Committee for Deukmejian, the governor, to either approve or disapprove. Historically, Deukmejian had vetoed all of them. So there was a wish list of twenty-one things, and mine was on the bottom.

Julie Krevans got David Gardner to call the governor's office, saying that for the city of San Francisco, not the university, to build a building for AIDS research was a great idea.

Hughes: Why are you emphasizing the city?

Sande: Because if the money had gone to UC, it would have been on the UC priority list, where there are probably thirty different priorities for buildings in the whole UC system. It would have been a difficult task to work that through this priority list of capital projects. But by going directly to the city to build at San Francisco General, the university could run it, and the city could build it, and the building could be a city building.

So we got Feinstein to politic Willie Brown; we got Krevans and Gardner to politic the governor; I politicked Vasconcellos--convinced him it was a good idea. To the surprise of many in Sacramento, the governor signed it. [laughter] And that's how I think we got this building. We forgot to ask for operating

expenses. Well, we wouldn't have gotten them. We promised not to ask for them when we testified before one of the other committees.

Then Mary Pitman, who's an absolute genius--she was president of the California Public Health Hospital Association, and now is back working at the national level in Chicago--sort of was responsible for seeing once the bill was signed that it didn't get clobbered by staff in these various places.

Hughes: What was her position then?

Sande: She was with the health department here in San Francisco. So now it became a health department issue, because they got the money.

Hughes: I was going to ask why a basic science institute was located at San Francisco General. There was never a chance of it going to Parnassus [UCSF]?

Sande: Oh, no.

Hughes: Which is a big thing!

Sande: Incredibly important for this institution, absolutely. Then to have hired Warner Greene to run it was absolutely phenomenal.

Hughes: UCSF is the basic science campus, and SFGH is the applied clinical science campus.

Sande: Not any more. I don't think so. I think we have built basic science down here now to a position of really international eminence. We have the Rice Liver Laboratories, the Lung Biology Center, the Gallo Research Center for Neurology. We have the Infectious Disease Laboratories, we have the two Gladstone institutes--it's an absolutely incredible institute now.

Hughes: Does this cause tensions with UCSF?

Sande: Sure. Well, we are UCSF. Parnassus is a part of UCSF, just like we're a part of UCSF.

Hughes: [laughs] They'd love to hear you put it that way.

Sande: I do it all the time.

Delayed Federal Funding

Hughes: Do you want to say something on the subject of federal money?

Sande: Not really. [laughter] I didn't have much to do with it until I got put on the council of NIAID [National Institute of Allergy and Infectious Diseases].[1]

Hughes: I was thinking of the earlier period when some people contend that federal money for AIDS research was very slow in coming. Did you feel that, and if so, why?

Sande: I don't know why it was. It was slow in coming. And when it came, because of the state investment in AIDS research here, our investigators were right at the front edge of being competitive for those grants. They still are. I mean, everybody out here really were in a strong negotiating position.

The San Francisco Model of AIDS Care

Hughes: Well, let's turn to the so-called San Francisco model of AIDS care. Could you define it in your own words?

Sande: [laughs] I don't even know what it is any more. I think that what is unique about San Francisco is the gay community, and the incredible outreach--reaching out--that went on between members of the community. This led to an awful lot of unsolicited support systems that emerged and developed: the Shanti Project, the AIDS Foundation, hospice care, and everything. So when you're faced with treating a lethal disease like a malignancy, where would you want that care to take place? You'd like to have that care take place where there's a minimum of trauma, where there's a maximum of comfort for the patient.

So using community-based support systems, using the outpatient department as the major generator of delivery of acute medical care, minimizing inpatient stays, only putting patients in the hospital when they can't function in these areas--

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[1] Sande was a member of the National Advisory Allergy and Infectious Diseases Council from 1987 to 1991.

Sande: --became the San Francisco model. And it was sort of a marriage between the mayor, the city department of health, with their resources, our inpatient ward, our outpatient clinic, and these multiple support systems. It also allowed a lot of clinical investigation to occur. In a disease where you don't know the answers, where there is no obvious cure, there's a tremendous incentive for patients to want to go where they're doing clinical trials, because one of those things that they're studying might be the cure, might be the answer. So that made us very attractive for patient care. So that's my explanation.

Hughes: How successfully has the model been translated elsewhere?

Sande: Well, where there are resources and where there are good community services, it has been successful. But not very well in New York. Not very well in the big cities where this is a different disease completely.

Hughes: If the gay community is an important ingredient of this model, it has implications for other cities, but maybe also for San Francisco eventually, since the face of the epidemic is changing.

Sande: We're seeing that here, too.

Hughes: Do you have any predictions about how the model would translate as the risk groups change?

Sande: Not as well.

Hughes: Is there anything that you can do about that now?

Sande: I'm not sure what's being done on that, because I'm not quite as close to it as I used to be. But as AIDS goes into the underserved portions of the population, I think we're doing a fairly good job in our primary care networks, in the city clinics, at reaching out to those people. But the problem is then, you don't have the manpower, the personpower, that you have when you have this whole group of people committing large blocks of their daily life to caring for others. And that's what the gay community really does, and did, maybe even more than they do now; it's been fairly decimated. But there's really just an outpouring of commitment. That's what probably made it more possible than resource allocation or clinics that you pay people to work in. It was the volunteer work that was particularly important.

Burnout

Hughes: I've detected a similar commitment amongst the physicians, that the rest of life was put on hold, so to speak. Does that fit what you remember of those early years?

Sande: Yes. That's why there's a lot of burnout.

Hughes: Why was there such willingness to turn personal lives upside down?

Sande: Well, a lot of the physicians involved were, and still are, gay physicians, and a large number of these highly committed--but not all of them. Others were just committed because they were caught up in an incredibly depressing situation.

Hughes: Was there also a feeling of "us against the epidemic," that a battle was being waged, and they had to stick with it?

Sande: I think so. And I think that helps to explain the [County] Community Consortium, which Donald Abrams runs. He brought together seventy to 100 physicians in San Francisco who cared for AIDS patients to do clinical trials. I think there is a tremendous sense of camaraderie and esprit de corps among that group. And these are guys who are doing most of the AIDS care in the city, and who do have a lot of burnout. So this consortium has been a resource for them to share their miseries and share their successes, and help bond together to do clinical trials, or help solve the epidemic, in a little way, shape, or form.

Hughes: Are there also more formal ways of dealing with burnout, specifically here at the hospital?

Sande: Here, there are support groups. They meet on a weekly basis to talk about patients, talk about their own problems. That's been handled quite well. I think Paul has done a great job in organizing the clinic, and he's had really good people to run it--Michael Clement, who's gone into practice over in Oakland, and now John Stansell.

More on the Relationship between the AIDS Clinic and Ward, SFGH

Hughes: Talk more about the relationship between the clinic and the ward, and the tensions that must have arisen, and probably still do.

Sande: There were tensions because there was a lack of communication. Typically, the clinic would start running down at four-thirty on a Friday afternoon, and they'd have all these really pretty sick people who hadn't been seen. So the natural tendency was to want to admit them over the weekend to tune them up a little bit. And initially there was not much communication between the providers in the clinic and housestaff, and the attendings here on the wards. It was really because of that need that Paul and I hired Michael Clement.

Hughes: Who was to serve as a liaison?

Sande: He was the communicator. His job was to communicate between the clinic and the ward, to bridge the gap, and he did it beautifully, just beautifully. He is a gay physician who came from Portland [Oregon] with training in internal medicine, and has an absolutely winning personality. I wonder what year we hired him? I would think '86 or '87. Then he became head of the clinic after that, and then he gave it up to John Stansell.

We get consultations on all the AIDS patients by this "service," in quotes, of AIDS docs who are on 5A, who are the link to the outpatient clinic. That was a very important thing, to do that, because that really dissolved the tensions that we had because of lack of communication. That worked beautifully; one of the few things that's really worked well.

Patient Care

Hughes: Is there anything to be said about the evolution of patient care? How did patients experience their suffering and how did the staff respond?

Sande: I don't think I am close enough to say now. I'm probably the wrong person to ask.

Hughes: I'll ask Connie Wofsy.

Sande: Connie might be good. Maybe people like Lorrie Kaplan, John Stansell.

Hughes: You used to deal routinely with AIDS patients?

Sande: I have never had an outpatient practice in the clinics here. I've always dealt with them on the wards. So on a daily basis, I have not been as close to the actual care of AIDS patients as the

people that work for me. I hear about it here every morning at report, when inpatients are presented to the other residents, the assistant chief, and myself. I see them on the wards. I attend like I am doing right now in infectious disease when I take care of them. But that's why it's just great when I get up in front of a large group of people and say, "This is the way we treat these things," and all the people in the audience who really know sort of snicker and say, "Baloney." [laughter] So that's my true confession.

The Epidemic's Effect on Medical Education

Hughes: How has the epidemic changed American medicine?

Sande: That's too broad a question, but let me focus on one part of it that I am particularly involved in or sensitive to, and that is how it has changed medical education. I think it's actually been very good for the focus and the way we train young doctors. I have a perception, beginning when I was in training, that we got increasingly enamored with technology, with our ability to put in pacemakers and EKGs all the time in the wards, and document the pathophysiology of the arrhythmia and all these sorts of things. We worked very, very hard for our patients, and a death was a terrible failure.

And what's happened with AIDS is we [physicians] have come to realize that this is a dying population, this is a dying patient. But then we're all in the process of dying. So I think we have become much more sensitive to quality-of-life issues, of dealing with the human part of the patient. I think it's brought the art of medicine back into our medical education process. The idea of orchestrating a good death, which would have been an oxymoron in my days of training, has now become a real endpoint. And if we can teach our physicians to consider a death of a patient who is at peace, whose estate has been handled, who dies without pain, who dies without loneliness, as a major success, as an A+, then we have made a tremendous impact and a positive statement. And I think that's what AIDS has done to us.

I think it's brought us face to face with our own personal--that's not the right word--we are very mortal. We are able to do only so much. It has, I think, helped our reality testing and how much we can do and how well we can do it. I think that's very important. I think we've become more sensitive, more concerned about the patient as a patient and not as a test tube. I think that's good. So I think AIDS has had a major impact on that.

Hughes: You're speaking in a broader sense than impact strictly on AIDS medicine?

Sande: Yes. I think it spills over to everything. That's why I think taking care of AIDS patients for housestaff is a very, very important and rewarding experience from that standpoint.

Hughes: Is it a hard orientation for a medical student or an intern or resident to adopt, because that isn't, as you've been saying, the thrust of medical education?

Sande: I think it's happened. No, I don't think it's difficult. I think from the very beginning they are learning the limitations of their own abilities to positively alter these processes.

Physician-Patient Relationships

Hughes: Do you want to say anything specifically about the impact of the epidemic on the physician-patient relationship?

Sande: I think there are tremendous personal rewards for physicians who care for AIDS patients. This is not what the general perception has been. But I think if you have the attitude that you can significantly affect the quality of life of the AIDS patient, and that you focus on that, that there will be tremendous rewards for the individual physician.

Now, this is where it gets very tricky in terms of the changing patient population. In this hospital, when we took a survey about four or five years ago, "What are the patients you most like taking care of?," it was the AIDS patient as number one. Not what you would have predicted, but that's true. Because in our hospital it tended to be an intelligent, communicative, thankful patient population that brought that feeling of thanks to the house officer.

Now--this might sound bad--because of the nature of the intravenous drug user, the hardened addict who contracts AIDS, that population tends not to be as thankful, pass along those feelings to the house officer. Now, that's a generalization, and they're always dangerous, but in general, I think that's probably true. So that may alter the dynamics to a certain extent.

Hughes: Has your engagement in the epidemic meant more than just a series of medical and scientific problems?

Sande: Yes, I think I've just articulated that. I think it's made us better doctors in the traditional sense of the word. That is an area that has not received enough play, enough visibility, enough publicity. This maturity, this learning one's limitations and learning one's mortality has been a very important issue.

Failure to Move AIDS Science to the Bedside

Sande: I think it's done another thing. I recently chaired a consensus committee back in the NIH in Washington on antiretroviral therapy, which was published in JAMA a couple of weeks ago.[1]

Hughes: Yes, I saw that.

Sande: This is hard to say correctly--but among basic scientists who are really good, who are really creative and tough, hard-nosed scientists, there is an obvious arrogance. And you know what I mean.

Hughes: Yes.

Sande: If there has ever been a disease that should destroy that arrogance, it's AIDS. Because while we have gained incredible insight into how the virus works, incredible insight into the molecular biology and how the regulatory genes create, and how the immune system turns on, how the signalling happens, that has essentially in no way, shape, or form, been translated to the bedside. There is a tremendous gap.

In fact, I was just quoted in the New York Times about three or four weeks ago by a fellow who died of AIDS who was the reporter for the New York Times. He interviewed me last summer, and I was talking about this. He said--that was my quote, and I loved it, because it's so true--that we're in an in-between phase between the generation of the scientific information and the translation to the benefit of the patients. Vaccines haven't worked; therapy hasn't worked very well.

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[1] M. A. Sande, C. C. J. Carpenter, et al. Antiretroviral therapy for adult HIV-infected patients. Recommendations from a state-of-the-art conference. Journal of the American Medical Association 1983, 270, #21, 2583-2589. See also: Lawrence K. Altman, Government panel on H.I.V. finds the prospect for treatment bleak. New York Times, June 29, 1995, p.63.

The most important single observation is one that Margaret Fischl made where she started using trimethoprim sulfa prophylactically against Pneumocystis. That's probably given more prolongation of life than any of the multi-millions of dollars that have been spent on AIDS. So there should be an honest self-evaluation by these brilliant people.

Hughes: Humility, maybe.

Sande: Humility! Humility was the word I was looking for. That was the word I used. There should be a tremendous humility emerging in our basic science community in terms of their inability to make significant progress in translating the basic science information to the clinical arena.

Hughes: Has there ever been an instance in the history of infectious disease where so much of the science was known and so little clinical application?

Sande: That's an interesting question. I guess one area might be malaria. There's been a series of failures in vaccine development. I think polio worked, but polio is a simple virus.

The Media

Hughes: Do you want to say something about the media's role in this epidemic?

Sande: There were the good guys and the bad guys. [laughter] My hero and very close friend is Larry Altman, who I talk to a lot. He's got his hangups, like peer review, but he really has handled himself very admirably and some day should be rewarded for his reporting of this epidemic.

Hughes: In terms of what qualities?

Sande: Interesting question. He is precise and accurate to a fault, very thorough, very searching comments, searching journalism. Why is it, why doesn't this work? He was so taken by the observation that three drugs in a test tube worked, killed the virus, because the final mutation necessary for emergence of resistance to the last drug was a lethal one. This was the thing that Marty Hirsch reported. Larry was so taken by that, and then he started to hear rumors that there was problems with it. And then other people couldn't confirm it.

And then it turned out that they didn't use the right controls. Larry kept probing: "What happened? Why did this happen?" They finally admitted that they just didn't use the right control. Marty came across and said, "I'm sorry; I made a mistake." And it was dropped.

Hughes: Did Altman speed that process along?

Sande: I think so. He is a hero of mine because he is totally honest, to a fault, as I read him. I've known him since 1969, I guess.

Hughes: What do you mean by "honest to a fault"?

Sande: He's a guy who I think has no other ambition in life than to be a reporter and to seek the truth. He traveled through Africa before any of the African nations would agree they had AIDS, and he reported on it. He became persona non grata, at some great personal risk to his own life. He just pushed, pushed, probing, probing, probing. I just love him. I read him all the time.

Hughes: You're saying that he does not bend stories for political ends? He reports as he sees it?

Sande: As he sees it. And he doesn't exploit the sensationalism, like others do. What I admire about him is his honesty, the way he probes.

Hughes: You have been pulled into the political process in a disease which probably is the most political that has ever existed. How do you feel about that politicization?

Sande: Well, I guess it's a two-edged sword. The money to study the disease comes from the political process. Without the advocate groups, without the political pressures put on, there never would have been this much money this quickly, even though we all say it was too slow. So in a way, the political process has been a very positive process for trying to find solutions to a very complicated problem. I was amazed at the testimony by the advocacy groups before this committee that I ran in Washington. They just flip-flopped totally, 180 degrees, about placebo controls. What they're saying now is that, "We want the truth. Do the drugs work or don't they work? We want the truth."

Before, they were saying, "Study all the drugs. We want to be part of your studies. We want to get the drugs. We don't want placebos; we just want the drugs." There's been a total change in that mentality. Now they realize that uncontrolled trials have given--bad science gives bad results, gives bad answers, gives inconclusive answers. What we were faced with in writing this

consensus report is that a lot of the trials didn't answer the questions. Now they're saying, "We want the answers." But you can't fault the advocacy groups, because particularly back then, they were hoping for a quick cure, a quick solution.

Hughes: One of the main messages of that paper was that there aren't any fixed answers. It's not even certain when treatment should begin, if at all.

Sande: That's true.

Hughes: So that's an evolution in medical thinking about AIDS therapy, right? AIDS physicians as a group used to be quite doctrinaire about early intervention.

Sande: We wanted simple answers to complex problems.

Sande's Contributions

Hughes: What do you consider your greatest contribution to the epidemic?

Sande: Hmm. I guess as the facilitator of development of this institution to the national prominence that we've achieved. Which is what my job is. I mean, that's what I was hired to do, to try to bring this place into national prominence. I don't think I could have done it without AIDS. I think that AIDS was a vehicle --it's a crass way of saying it--it was an opportunity for somebody with my background in infectious diseases to take hold of it and run with it. I didn't do any of these things myself. I was the facilitator. I was the person who made it happen through other people.

My own contribution in a more personal way is as a communicator, as a person who tried to produce for the practicing physician or for the public, a comprehensive view and understanding of what the scientists were saying. So I look at myself as an interpreter of the science for the clinician. That's why our AIDS book has done well.[1] We felt it was important that doctors knew how to care for AIDS patients, and if we were able to show them what the real pros were doing, communicate that to them, that they would feel comfortable in caring for AIDS patients and

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[1] The Medical management of AIDS. M. A. Sande and P. A. Volberding, eds. Philadelphia: W. B. Sanders Co., 3rd Ed., 1992.

they wouldn't fear them. So I guess those two things I consider to be my contributions.

I've enjoyed writing papers on new clinical descriptions of AIDS with my chief residents over the years. We had a lot of good publications in the New England Journal [of Medicine]. Some have been greatly criticized. We've had this incredible patient population, and I think we have maximized the use of it for scientific development.

Hughes: Do you look upon the hospital's standing as the leading AIDS hospital in the country as an affirmation of your ambitions for the institution?

Sande: Yes, I think so. I think that it took a lot of people to do that, and I was only part of the picture. I hired good people and I supported them. I hope that I let them grow and develop without any hindrance, which I think is tough to do sometimes. I would hope one of my personality traits that has allowed me to do that is that I'm secure enough that I don't need to get in the way. So I can derive tremendous personal satisfaction in seeing people develop and emerge, and in helping them and guiding them and supporting them when they need support, and thrashing them when they need to be thrashed.

That's what the role of chairman of medicine should be, I think. I try to emulate other people that have trained me and I've worked with. What I think I'm proudest of is to see these people develop. That's why I love this course [Clinical Care of the AIDS Patient] that we just had in December, three days, 600 physicians from all over the country come to hear our people. Ninety percent of the program was [made up of] people from San Francisco General Hospital and UC. It's really neat. It's a showcase of our accomplishments.

Hughes: Well, I thank you.

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

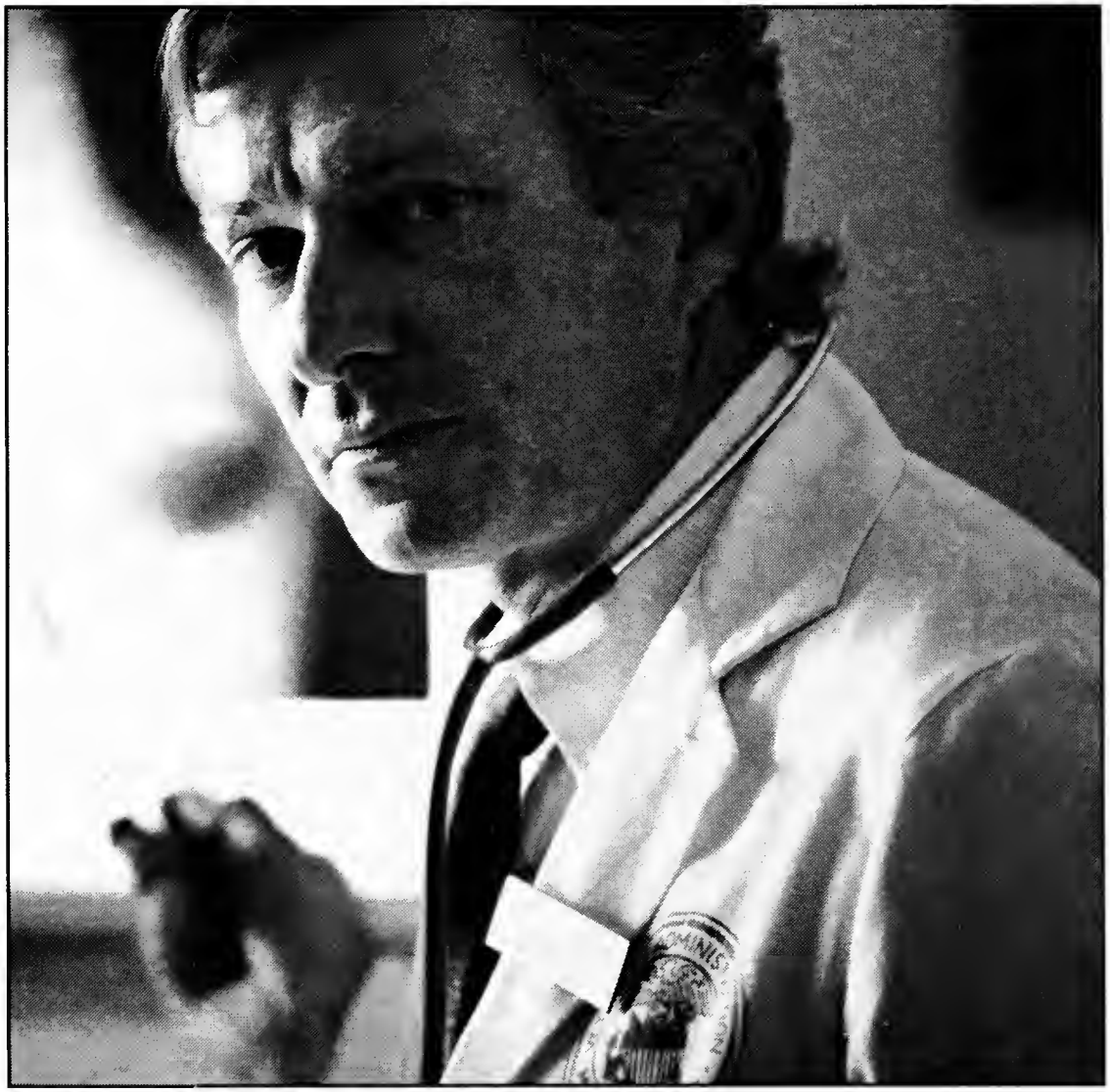
THE AIDS EPIDEMIC IN SAN FRANCISCO: THE MEDICAL RESPONSE, 1981-1984

Volume IV

John L. Ziegler, M.D., Ph.D.

ONCOLOGIST: KAPOSI'S SARCOMA AND AIDS RESEARCH IN SAN FRANCISCO AND GLOBALLY

Interviews Conducted by
Sally Smith Hughes
in 1994



John L. Ziegler, 1988.

Photograph by David Powers

Interview History--by Sally Smith Hughes, Ph.D.

John Ziegler, a physician and oncologist, was the most senior clinical scientist of the faculty members at UCSF and San Francisco General Hospital [SFGH] who in the summer of 1981 became involved in the epidemic of immune deficiency, later christened AIDS, which was just being recognized in gay men in San Francisco, Los Angeles, and New York City. Ziegler arrived in San Francisco in August 1981 to assume positions as Associate Chief of Staff at the Veterans Affairs Medical Center in San Francisco and as Professor of Medicine at UCSF. By then, he had accumulated almost fifteen years of experience in cancer research and treatment at the National Cancer Institute [NCI] of the National Institutes of Health. Ziegler's career-long interest was in the lymphomas and Kaposi's sarcoma, forms of cancer which he had studied not only at the NCI but also on a five-year sojourn in Africa as an NCI Senior Investigator.

As Ziegler recounts in his oral history, within days of his arrival in San Francisco, he heard of cases of Kaposi's sarcoma occurring in young patients being treated at the university. He was immediately interested, especially since Kaposi's in the West is usually found in elderly men or patients immunosuppressed by chemo- or radiotherapy. These patients fell into neither category. He consulted Paul Volberding and Marcus Conant, physicians seeing these patients, and attended the first meeting of the Kaposi's Sarcoma Study Group at UCSF, which the two physicians co-directed. As Ziegler explains in his oral history:

> We put our heads together and we first of all figured out that we needed some funds to get started studying this epidemic of Kaposi's sarcoma. There was no money, and the university really wasn't coming up with anything at that time, because nobody knew what [the epidemic] was and whether it was worth pursuing.

With the advantage of his reputation and professional contacts in the cancer field, Ziegler orchestrated what most likely was the first grant awarded anywhere for AIDS activities. The $50,000 received from the American Cancer Society on November 1, 1981 supported a nurse-coordinator for the Kaposi's Sarcoma Clinic at UCSF.

Six months into the epidemic, Ziegler began to notice the occurrence in AIDS patients of a second type of cancer. In 1982, he and his San Francisco colleagues published a paper on "Burkitt's-like lymphoma in homosexual men," which constituted the first report of the association of malignant lymphoma with AIDS. However, it took two years, a more extensive study (which Ziegler coordinated), and a publication in the prestigious New England Journal of Medicine to persuade the CDC to include lymphoma on its list of AIDS-defining conditions.

Among the other topics which Ziegler discusses are the many hypotheses about AIDS etiology circulating in the early days, speculation that was more or less settled in 1984 when the U.S. Secretary of Health officially announced the isolation of a virus, later named the human immunodeficiency virus or HIV.

The Oral History Process

Two interviews were conducted with Dr. Ziegler, a man distinguished in appearance and address, on January 28 and February 16, 1994, in his unpretentious office in the Nursing Home at the Veterans Administration Medical Center. The sessions were hastily scheduled so that they could be concluded before Dr. Ziegler's departure for sabbatical leave in Africa, where he was returning to pursue a new theory about the cause of an indigenous form of Kaposi's sarcoma. The interviews were abetted by research in Ziegler's papers, which have since been transferred from the VA to the AIDS History Project Archives at UCSF Library. A short telephone interview conducted with Ziegler in 1990 by the NIH Historical Office served as orientation to some of the features of Ziegler's AIDS efforts.[1] Articulate and thoughtful, Dr. Ziegler was an apt and engaged subject. The edited transcripts were sent to Africa for his review and returned with minor corrections and additions.

This is the oral history of a man who because of his position as a full professor and his long experience and solid reputation in academic oncology--he is a recipient of the prestigious Lasker Award (1972)--added weight and substance to the initial group of UC AIDS researchers. Young, inexperienced, and handicapped by the stigma associated with AIDS, they benefited from Ziegler's standing in the eyes of colleagues and funding agencies.

But AIDS work also changed Ziegler. He describes how as co-chairman of the Sixth International Conference on AIDS, meeting in San Francisco in 1990, he joined the activists in protesting the Bush administration's dictum that conference attendees from abroad be tested for HIV. "In the end, when we joined hands with the AIDS activists and walked down Market Street [in downtown San Francisco], it was the first time in my life I had ever taken to the streets for a cause. And I must say, my heart was in it by that point."

The Regional Oral History Office was established in 1954 to augment through tape-recorded memoirs the Library's materials on the history of California and the West. Copies of all interviews are available for research use in The Bancroft Library and in the UCLA Department of Special Collections. The office is under the direction of Willa K. Baum, and is an administrative division of The Bancroft Library of the University of California, Berkeley.

Sally Smith Hughes, Ph.D.
Research Historian

Regional Oral History Office
April 1997

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[1] I thank Victoria Harden, Ph.D., director of the NIH Historical Office, for arranging to send the transcript of the telephone interview conducted with Ziegler on January 5, 1990.

Regional Oral History Office
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BIOGRAPHICAL INFORMATION

(Please write clearly. Use black ink.)

Your full name JOHN LEVERETT ZIEGLER

Date of birth 28-10-38 Birthplace NEW YORK NY

Father's full name RUSSELL A ZIEGLER

Occupation ADVERTISING Birthplace SOUDERTON PA

Mother's full name HELEN MEARS ZIEGLER

Occupation HOUSE WIFE Birthplace WILLIAMSTOWN MA

Your spouse RUE WINTERBOTHAM ZIEGLER

Occupation ARCHITECT / ANTHROPOLOGIST Birthplace SAN FRANCISCO CA

Your children ANN ZIEGLER (30), BILL ZIEGLER (28)
KAREN ZIEGLER (26) JOHN ZIEGLER (23)

Where did you grow up? NEW ENGLAND (CONNECTICUT, MASS.)

Present community MARIN COUNTY

Education HOTCHKISS SCHOOL, AMHERST COLLEGE (BA ENGLISH LIT) CORNELL UNIV. MED. COLLEGE, (M.D)

Occupation(s) PROFESSOR OF MEDICINE (UCSF). SENIOR SCIENTIST, WORLD HEALTH ORGANIZATION

Areas of expertise CANCER, AIDS, EPIDEMIOLOGY, INTERNAL MEDICINE, MEDICAL EDUCATION

Other interests or activities MUSIC, SPORTS, READING, ENOLOGY

Organizations in which you are active TRUSTEE EMERITUS MARIN COMMUNITY FOUNDATION

I EDUCATION AND EARLY CAREER

[Interview 1: January 28, 1994] ##[1]

Medical Training, 1960-1966

Hughes: Dr. Ziegler, please start with your education and early career.

Ziegler: All right. My involvement with the AIDS epidemic really does begin way back. I went to Cornell Medical School [1960-1964] and Bellevue Hospital [New York, 1964-1966], where I did my training. I think training in Bellevue Hospital gives you a taste of what third-world medicine must be like, because of the deprivation and the poverty and the problems with indigent patients. Then I went to the NIH, the National Cancer Institute, where I was inducted in 1966 with many other doctors who wanted to do research and not go to Vietnam. So I ended up in the Public Health Service.

I had encountered a patient with Burkitt's lymphoma when I was training at Memorial Hospital in New York. Burkitt's lymphoma is an unusual childhood cancer that was reported by Denis Burkitt in Africa in the early sixties, and it was a fascinating problem from many points of view, but one of the most interesting facets was that this tumor could be cured by chemotherapy.

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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.

Clinical Associate, Medicine Branch, National Cancer Institute, 1966-1967

Ziegler: So when I arrived at the National Cancer Institute as a young associate in 1966, they asked me if I had special interests in certain kinds of cancer, and my response was that I was very interested in Burkitt's lymphoma, because of the unusual cure rates and the fact that I had encountered a patient at Memorial Hospital. So one thing led to another, and I was asked to look into the possibility of setting up a small cancer treatment unit in Uganda, funded by the National Cancer Institute. The first year, I worked with Dr. Paul Carbone, Dr. [Vincent] Devita, and Dr. Zubrod at NIH, and Dr. Burchenal from Memorial Hospital. All of these men were pioneers in cancer chemotherapy. They were all very interested in why Burkitt's lymphoma was curable.

Director, Uganda Cancer Institute, Makerere University Medical School, Kampala, Uganda, 1967-1972

Ziegler: To make a long story short, the project was approved, I went to Uganda in 1967 with my family, and worked there for five years on Burkitt's lymphoma (this childhood tumor that is curable). Along the way I became interested in another indigenous African tumor called Kaposi's sarcoma. Now, this is a tumor that's exceedingly rare in developed countries and the West, but in Uganda comprised nearly 8 or 9 percent of the adult malignancies. So it was a very common tumor. For the five years from '67 to '72, I and many colleagues from the National Cancer Institute and elsewhere worked on these indigenous African tumors. Other tumors that were interesting there were liver cancer, melanoma, malignant melanoma, and other childhood cancers.

Hughes: In much greater prevalence than here?

Ziegler: Much greater prevalence, yes. Liver cancer, for example, accounts for half of the malignancies in many African countries.

The other interesting thing about this group of malignancies was that they were becoming more and more related to viruses. Burkitt's lymphoma was linked with the Epstein-Barr virus, a virus that we now know causes infectious mononucleosis. It's also linked with several other forms of cancer. And liver cancer, of course, is linked with the hepatitis viruses. And we thought Kaposi's sarcoma [KS] at the time might be linked with a virus, but nobody could figure out which one. There was some

suggestion that it might be cytomegalovirus, one of the other [herpes] viruses.

Hughes: Why did you think that in the first place?

Ziegler: Well, because Kaposi's sarcoma is clustered in certain parts of Africa. It occurs in generally high, wet areas, not in low, dry areas. It was spotty in the country where I was working, for example; more than two-thirds of the cases came from the western side of Uganda. So there were some geographical peculiarities which we couldn't figure out. But in the end, after five years in Africa, my career had really centered on the indigenous tumors of tropical countries, and I wrote quite a few papers about that.

Then I left. Idi Amin came to power in Uganda in 1971, and he was, as everybody I think knows, a real tyrant and plunged the country into a desperate economic situation which resulted in a civil war lasting all the way up until 1986. After I left Africa, I kept up with my colleagues there. Fortunately, we had trained a number of Ugandans who took over and kept up the research that we had started in an institute called the Uganda Cancer Institute, which is still running today.

Return to the National Cancer Institute, 1972-1980

Ziegler: I went back to the National Institutes of Health, to the National Cancer Institute, took several positions there leading various groups--first, pediatric oncology [1972-1975] and later clinical oncology [1975-1980].

Associate Chief of Staff for Education, Veterans Administration Medical Center, and Professor of Medicine, University of California, San Francisco, 1981-present

Ziegler: In 1981, I was invited out to San Francisco to take over a job as associate chief of staff for education here at the VA, and also to become professor of medicine at UCSF.

Hughes: How did that come about?

Ziegler: I had been at the NIH for about fifteen years, and I was ready for a career change. My former professor of medicine, Marvin Schlesinger, who's still here, found me and invited me to come

out and look at a job here at the VA. It was too good to turn down.

Hughes: Did they want a research-oriented person?

Ziegler: Well, they were starting an oncology division here; they wanted some help with oncology. I had a great interest in medical education. I had doubled my salary, and there were a lot of good reasons for coming here. I had remarried, and my wife [Rue] also was very interested in coming to the Bay Area, where her children were. So there were personal and professional reasons for coming.

II THE AIDS EPIDEMIC

Kaposi's Sarcoma in Gay Men

Ziegler: In the end, I arrived here in August of 1981, and I hadn't been on the campus but maybe a day when I got a call from somebody who said, "You know, there's a doctor down at San Francisco General [Hospital, SFGH] who's seeing a lot of cases of Kaposi's sarcoma, and we know you've done some work in it. Maybe you could get together." So I got together with Paul Volberding and Marcus Conant. Within weeks of my arriving, we had figured out that Kaposi's sarcoma was appearing in gay men for unexplained reasons, and that there was an associated immune defect in these patients. We put our heads together, along with John Greenspan and Donald Abrams and Art Ammann and quite a few other UC people.

Hughes: Had you seen the article in the MMWR [Morbidity and Mortality Weekly Report]?[1]

Ziegler: Yes, I had known about that. In fact, the first I knew about it was in the New York Times,[2] which had published a small piece about Kaposi's sarcoma in gay men.

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[1] Centers for Disease Control. Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men--New York City and California. Morbidity and Mortality Weekly Report 1981, 30, #25:305-307 (July 3, 1981).

[2] L. K. Altman. Rare cancer seen in 41 homosexuals. New York Times, July 3, 1981, p. A20.

Ziegler: About a week after that, I was called by Bruce Chabner who was then the head of the Division of Cancer Treatment [at the National Cancer Institute], because he knew I had known about Kaposi's sarcoma, and said, "We're having a meeting at the National Cancer Institute in September [1981], could you come? We want to have discussions about this thing." This was probably the first multidisciplinary workshop on what was to become the AIDS epidemic.

Hughes: Did it make any difference that the cancer aspect of the disease seemed to come to the attention of NIH first? Was the epidemic at first under the auspices of NCI?

Ziegler: Yes. In fact, one of the things in my CV, you may have noticed, is a report of that workshop, which is in The Journal of the National Cancer Institute.[1] That piece shows how naive we were at the end of the workshop; we hadn't a clue what was going on, not a clue. There were all kinds of guesses as to what Kaposi's was about. But you're right: The cancer caught people's attention. Then the infectious disease people quickly came in when they saw the Pneumocystis cases rising, and the cryptococcal disease and toxoplasmosis and all of the other opportunists.

Hughes: I remember from that paper that you came up with a staging system. But something else I read of yours gave me the idea that it was very difficult to stage KS.

Ziegler: It was, and it still is very difficult. It doesn't behave like the usual cancers in stage I, II, to III because it occurs in many places simultaneously. Most cancers start, for example, in the breast; they move to the lymph node; they move to the bone and the brain. So they march along in an orderly way. Kaposi's doesn't. And it doesn't necessarily spread in a particular way.

Hughes: Didn't you say everything telescoped in AIDS patients? That everything was moving much faster?

Ziegler: Yes, that's exactly right.

Hughes: How useful was the staging system that you came up with at the end of the workshop?

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[1] J. L. Ziegler. Kaposi's sarcoma in homosexual men. Journal of the National Cancer Institute 1982, 68:337-338.

Ziegler: Well, probably no less helpful than it is now. [laughs] There have been about eight different staging systems since then. But I think it all comes down to a couple of things: where Kaposi's appears and how it is spread is probably more a matter of what causes Kaposi's rather than any kind of intrinsic nature of the tumor. And also, of course, the host immune defense; people who have very bad immunity can have very widespread disease.

Raising Funds

Kaposi's Sarcoma Study Group

Hughes: Tell me about the Kaposi's Sarcoma Study Group which met at UCSF.

Ziegler: We started right away getting together and meeting in September [1981].

Hughes: Were you at the first meeting?

Ziegler: Oh, yes. Marcus Conant, I think, was probably the main leader, and Paul Volberding at the General [SFGH], and myself here at the VA, were the three principals. We put our heads together, and we first of all figured out we needed some funds to get started studying this epidemic of Kaposi's sarcoma. There was no money, and the university really wasn't coming up with anything at that time, because nobody knew what [the epidemic] was and whether it was worth pursuing.

The American Cancer Society Grant, November 1, 1981

Hughes: Had you explored getting university funds?

Ziegler: No, we actually hadn't at that time, because the university didn't have any particular pot of money with which to do this. I called an old friend of mine, the late Dick [Frank J.] Rauscher, [Jr.] who was the senior vice president for research in the American Cancer Society. I explained to him that we were seeing a kind of epidemic of Kaposi's sarcoma here in gay men, and could we apply for what they call a research development award, which

would have a very quick turnaround, and would award money for research in a matter of weeks.[1]

So Marcus and myself and others put together a protocol with myself as the principal investigator. We sent it to Dick Rauscher, and within a week he called to say, "$50,000 for a Kaposi's sarcoma clinic." And I think I would have to say, unquestionably, that's the first grant for AIDS in the United States, because the grant was awarded I think November 1, 1981.

So with that $50,000, we immediately hired a research nurse.

Hughes: Was that Helen Schietinger?

Ziegler: Yes, Helen Schietinger. Who's still in the business, and is an AIDS consultant now in Washington.

The National Cancer Institute Grant, May, 1983

Ziegler: So we started the clinic. Helen immediately saw the magnitude of the problem. We began to look elsewhere to see if we could get additional funding, and we approached the National Cancer Institute, and they responded.[2] We put in for a grant that would cover the expenses of the clinic plus some additional research. By that time, Andrew Moss had joined the team, and was very interested in looking at the epidemiology.

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[1] See Ziegler to Rauscher, September 23, 1981. (Ziegler papers, folder: AIDS-NCS grant, library, AIDS Resources Program Archives, UCSF.)

[2] Request for Cooperative Agreements Applications: RFA. Studies of acquired immuno-deficiency syndrome (Kaposi's sarcoma and opportunistic infections), National Cancer Institute. NIH Guide for Grants and Contracts, vol. 11, no. 9, August 13, 1982. (John S. Greenspan Correspondence, 89-011, carton 2, folder: Conant, MA: JG/Beckstead etc. 1982); Marcus A. Conant to Kaposi's Sarcoma Study Group, August 20, 1982. (Courtesy of Evelyne Lennette.)

Scientific and Medical Resistance to AIDS Research

Ziegler: I have to say that as we progressed, there were a lot of skeptics. People were saying, "You guys are barking up a funny tree with all this--what's going on?"

Hughes: What was behind that remark?

Ziegler: One of the interesting things about the early part of the epidemic was that many of the mainstream scientists in the university were reluctant to see this either as a major public health crisis, or even as a scientific paradigm and curiosity that was really worth going after. There were some very good scientists who did. There were also some very good scientists who simply ignored the epidemic altogether.

Hughes: Why was that?

Ziegler: I'll never know to this day exactly why that was. I think it was a combination of things. I think part of it was clearly the fact that in San Francisco it was almost 100 percent a gay disease. I think that there was a reluctance to get involved in gay diseases, for whatever reason. I just don't know what the other reasons might be. Obviously, many scientists were totally absorbed in their own fields and just didn't want to divert themselves.

Hughes: And it was always just a natural for you?

Ziegler: Well, it was an obvious thing for me, because it just fell right straight into my career path. I had already been interested in cancer and viruses, and now here's a cancer epidemic with yet another virus.

Cancer and Viruses

Hughes: What was the status of the viral theory of cancer? Was that a credible hypothesis?

Ziegler: Very much so. By that time, there were at least four viruses linked with cancer. There was the Epstein-Barr virus and Burkitt's lymphoma, which was probably the first, followed by liver cancer and hepatitis virus. By that time, there was some pretty good evidence that cervical cancer and ano-genital cancers were linked with the human papilloma virus. There was the

discovery of the HTLV, the human T-cell leukemia virus, in the late seventies by Bernie Poiesz and [Robert] Gallo. That was another tumor virus, although it didn't pan out to be causing as many tumors as people thought it might. It was responsible primarily for a rare form of adult leukemia.

So there were four viruses linked with tumors, and there was always Kaposi's sort of hanging out there--Kaposi's and a vague association with cytomegalovirus, although many people were skeptical about the data.[1] Of these virus-associated tumors, four of them are common in Africa. And with the association of immunodeficiency--I've always been interested in immunology and cancer anyway--AIDS was a natural for me.

Lymphoma Associated with AIDS

Ziegler: Within the first year of the epidemic, we noticed a number of cases of lymphoma in gay men who were mirroring the same kind of clinical features that we saw with Kaposi's sarcoma--usually a high-grade lymphoma, very often in gay men who had other immunological defects.

Six months into the San Francisco epidemic, it was clear we were getting another outbreak of another kind of tumor in gay men. Still at this time we had no idea that this was an immunodeficiency caused by a virus, but there were suspicions. So again, our group wrote up that experience, called an outbreak of Burkitt's lymphoma in gay men in San Francisco, which was really the first report of the association of malignant lymphomas with AIDS.[2]

Hughes: Now, when you say the group, are you talking about the KS Study Group?

Ziegler: Well, members of this KS Study Group: Donald Abrams and Paul Volberding, and I think that John Greenspan was a co-author on that. And a group of people from Mt. Zion [Medical Center] were

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[1] See the paper to which Ziegler contributed: W. L. Drew, M. A. Conant, et al. Cytomegalovirus and Kaposi's sarcoma in young homosexual men. Lancet, July 17, 1982, 125-127.

[2] J. L. Ziegler, W. L. Drew, et al. Outbreak of Burkitt's-like lymphoma in homosexual men. Lancet 1982, 2:631-633. John Greenspan was one of twelve co-authors.

getting involved--Larry Drew and others. That was the sort of mix and match of the original group.

Hughes: As I remember, Burkitt's lymphoma was not part of the original CDC definition of AIDS.

Ziegler: No, it was not. And when we reported this outbreak, the CDC didn't really pay too much attention to it. In November of '83, I was in Houston, Texas. I had just gotten an award [Heath Award] there at the M. D. Anderson Hospital. It was a big meeting on lymphoma. There I met up with Ben Koziner from Memorial [Hospital in New York City], with Alexandra Levine from USC [University of Southern California], with the doctors from M. D. Anderson Hospital, and a group from New York University, Linda Laubenstein and others. I said, "Look, are you seeing a lot of lymphomas as well in these gay men?" And they said, "Yes, we all are." I said, "How many do you see?" And they said, "Oh, we have fifteen or twenty cases."

So I said, "Well, now, look. Let's put it all together in one article. I'll coordinate all the responses; I'll send out kind of a questionnaire; you send me your clinical information." So we did that, and within a month, we had ninety cases accumulated from five big centers.

So I wrote that up, and sent that to the New England Journal.[1] Immediately before that was published, the CDC called me and they said, "Yes, we'll put high-grade lymphoma on the list of AIDS-defining conditions." So that was the next step after Kaposi's, as far as cancer and AIDS was concerned.

I guess the main contribution that I made in the early years was the Kaposi's sarcoma work,[2] and also the recognition of lymphoma as an AIDS-defining condition.

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[1] J. L. Ziegler, J. A. Beckstead, et al. Non-Hodgkin's lymphoma in 90 homosexual men. Relation to generalized lymphadenopathy and the acquired immunodeficiency syndrome. New England Journal of Medicine 1984, 311:565-570.

[2] See, for example: J. L. Ziegler, C. L. Vogel, A. C. Templeton. Kaposi's sarcoma: A comparison of classical, endemic and epidemic forms. Seminars in Oncology 1984, 11:47-52.

The Expanded Definition of AIDS, 1993

Ziegler: Although they have now added, in the 1993 expanded surveillance case definition of AIDS, invasive carcinoma of the cervix, I don't know if there are going to be any cases. That's sort of anticipatory.

Hughes: Why was it added if it is anticipatory?

Ziegler: My guess is that it was partly political. I think it had to do a lot with the fact that women in general were being ignored in the epidemic, that human papilloma virus and cervical carcinoma were closely linked, and it was clear that women with AIDS certainly had higher risk of cervical dysplasia, which is a precursor for carcinoma. So I think they felt comfortable in putting in cervical cancer as a potential AIDS-defining condition. But it takes many, many years to get cervical cancer, and so I think that anybody who would survive long enough to get it would be pretty unusual.

Hughes: Is that the only condition in the case definition which is linked exclusively with women?

Ziegler: You know, I don't know the answer to that. I'd have to look it up. But the CDC definition is pretty generic, and I think that is the only gender-specific one. But I couldn't swear to it.

Hughes: One of the cries of the women activists was that they were being ignored.[1]

Ziegler: Yes. But that is now being remedied.

The Kaposi's Sarcoma Clinic and Study Group, UCSF

Hughes: Well, go back to the KS Clinic. I understand there was quite a protocol for taking patient histories. The CDC also had a long questionnaire that it was using for epidemiological studies?

Ziegler: Yes.

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[1] See, for example: Gena Corea, The Invisible Epidemic: The Story of Women and AIDS. New York: Harper Collins Publishers, 1992.

Hughes: Were these two sets of questions independent, or did you incorporate the CDC questionnaire?

Ziegler: Well, before we started registering patients, we had just an informal group meeting every week, and it was pretty much Donald Abrams and Paul and Marcus and John Greenspan and Andrew Moss and myself. Art Ammann was a regular attender.

Hughes: Did Jay Levy come early on?

Ziegler: Yes, Jay was an early person. And then others came and went over the years.

Hughes: How unusual was it to have so many disciplines represented?

Ziegler: I think it was pretty unusual in that respect. I think we all came together because all of us had an interest in immunology. I think that was the one drawing card for everybody, and of course, immunology does cross many disciplines.

Hughes: What becomes of the KS Clinic? Does it die out?

Ziegler: Well, here's what happened. The KS Clinic was funded first by the American Cancer Society, later by the National Cancer Institute, and then still later Paul and I were co-principal investigators of a program project grant that got funded by NIAID [National Institute for Allergy and Infectious Diseases]. So we were able to sustain the, quote, "KS Clinic" at Moffitt [Hospital, UCSF] for a number of years. But obviously, AIDS clinics needed help in other parts of the institution that were not supported.

When we applied and got some NIH funds for the KS Clinic, they were clearly inadequate. The NIH team had come out, they had cut the budget way back, so we were kind of bereft. That's when Marcus Conant did a remarkable thing. He went to [California State Assembly Speaker] Willie Brown, and he said, "Look, we've got an epidemic here in San Francisco. We need special earmarked funds. This is a crisis. We have no way of coping with this crisis, because none of the established institutions are really addressing it." Frankly, I think the federal government--"too little, too late" was well applied. I just don't think they got on top of it until the latter half of the 1980s.

Hughes: What were the reasons for the delay?

Ziegler: I think turf and disinterest and disbelief and too little direct contact. The AIDS epidemic in Washington, D.C., for example,

didn't really accelerate until about '83, '84. So the geography wasn't there.

Characterizing AIDS

Hughes: But wasn't it also that what you were seeing demanded input from all these different specialties, and touched on them?

Ziegler: Well, yes, it did. And I guess the thing was that the AIDS diagnoses were anomalous. These were things that you don't see in everyday clinical practice. You would wait a lifetime to see one case of Kaposi's sarcoma, and now we had a clinic full of them. Lymphomas in immunosuppressed people, yes, relatively common, but only in kidney transplant clinics. So here we had suddenly an outbreak of lymphoma.

Then these other opportunistic infections popped up: Pneumocystis pneumonia, herpes, cryptococcal meningitis, and so forth. It was pretty obvious within a few months that we were dealing with a very serious immune deficiency.

Hughes: Did that realization come from the lab work?

Ziegler: Oh, yes. Art Ammann's group quickly showed, along with many others almost simultaneously, that CD4, T4 helper lymphocytes were low in these patients, and that something funny was going on with these lymphocytes.

Then there were lots and lots of theories that cropped up, and we were working with the CDC. I think the CDC was hot on the trail of an acquired immunodeficiency that was spread from person to person, and they did some very classic studies, really nice studies, in Orange County and L.A. where they drew a lot of connections between the different gay men who were getting the disease, showing that there were many commonalities--not only common partners, but common practices, and a great deal of promiscuity that really characterized this huge cluster in L.A.[1] And then Andrew Moss began to find the same things here in San

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[1] S. Fannin, M. S. Gottlieb, et al. A cluster of Kaposi's sarcoma and Pneumocystis carinii pneumonia among homosexual male residents of Los Angeles and Orange Counties, California. Morbidity and Mortality Weekly Report 1982, 31, #2, 305-307 (June 18, 1982).

Francisco a little bit later.[1] So we were pretty much convinced that there must be some infectious agent.

And then in the fall of '83, [Luc] Montagnier wrote his paper in the Lancet that showed that LAV [lymphadenopathy-associated virus] was the causative virus, and then Gallo's papers six months later came out.[2]

The Baby with Transfusion AIDS, UCSF, December 1982

Hughes: Well, there was something else here at UCSF that convinced a lot of people that it had to be a virus, and that was the baby with transfusion AIDS.[3] Remember?

Ziegler: Art Ammann's patient, right.

Hughes: And that was December of 1982, before Montagnier and Gallo published.

Ziegler: Yes, that was a very important thing. Art and--who is that other fellow in UC pediatrics?

Hughes: [Morton J.] Cowan?

Ziegler: Yes. And Diane Wara. But Art Ammann I would have thought was the main UC person early on, and that baby was a classic. Then the blood bank groups started noticing that there must be something in the blood. And then everybody said, "Well, my god, could this be hepatitis?" It was looking for all the world like hepatitis--sexually transmitted, blood transmitted, vertically

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[1] A. R. Moss, P. Bacchetti, et al. AIDS in the "gay" areas of San Francisco. Lancet April 23, 1983 (letter).

[2] F. Barre-Sinoussi, L. Montagnier, et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (ADS). Science 1983, 220:868-871; R. C. Gallo, S. Z. Salahuddin, et al., Frequent detection and isolation of cytopathic retrovirus (HTLV-III) from patients with AIDS and at risk for AIDS. Science 1984, 224:500-503, and two additional papers by the Gallo group in the same issue of Science.

[3] R. O'Reilly, D. Kirkpatrick, et al. Unexplained immunodeficiency and opportunistic infections in infants--New York, New Jersey, California. Morbidity and Mortality Weekly Report 1982, 31:665-667 (December 17, 1982).

transmitted. Could it be hepatitis? And there was a flurry of excitement when somebody in Girish Vyas's lab found hepatitis virus in lymphocytes, but that completely fizzled out. But anyway, those were the days in which we were all thinking infection.

Hughes: How were you linking the lymphomas and KS with the opportunistic infections and what you were learning from the epidemiology and blood transmission?

Ziegler: Well, the biology was pretty straightforward, because we've known for years that lymphomas and Kaposi's sarcoma prey on people who are immunosuppressed. That was known before the AIDS epidemic. In renal transplant cases and in patients who get lots of corticosteroids, Kaposi's sarcoma occurs much more than you would see ordinarily. That doesn't mean it's terribly common, but for a very rare disease, when you see a lot of cases, it becomes unusual. So we had always linked Kaposi's with some form of immunosuppression.

The lymphomas had also been known to prey on people with immunosuppression--renal transplants, and other organ transplants, and so forth. So the cancer-AIDS connection, of course, was through the immunodeficiency link. That was pretty clear. The only question was whether the virus that was causing the immunodeficiency had anything to do with the cancers. And quickly after the virus was discovered, it was determined that the virus was not in any way involved directly with the Kaposi's sarcoma; they couldn't find the virus in the lesions. Nor could they find it in the lymphomas. So it was obviously a two-step process in the causal chain--the virus, immunosuppression, lymphoma.

Immune Overload

Hughes: Did you ever give any credence to some of the other theories that were floating around? Immune overload, for example?

Ziegler: Yes. Actually, Jay Levy and I wrote a paper before the virus was discovered.[1] It was a sort of accepted theory at the time that somehow gay men, because of their immense promiscuity, were

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[1] J. A. Levy, J. L. Ziegler. Acquired immunodeficiency syndrome is an opportunistic infection and Kaposi's sarcoma results from secondary immune stimulation. Lancet, July 9, 1983, 78-81.

overloading their immune systems with viruses and amoebas and various other things. Then we tried to explain the same thing by saying that it was immune overload in hemophiliacs, and immune overload in people with blood transfusions, and immune overload in IV [intravenous] drug abusers who were continuing pushing foreign antigens into their bloodstream.

But if immune overload were the case, why would the epidemic start in 1981 when these people had been immune overloaded for decades? So although immune overload was always held out as a co-factor, and I think it probably is a co-factor, the concatenation of all of those things simply didn't explain the explosive rise of the epidemic.

Hughes: Did that worry you at the time when you and Dr. Levy put forward the secondary immune stimulation theory?

Ziegler: Yes. I think we were all a little skeptical of it, and it was a little too facile, because it didn't explain why it should occur almost as a point-source of the epidemic.

Hughes: This was 1983 and public fear and health care worker fear of AIDS was at a pretty high level. Was there an element behind the theory of trying to pacify the public, because one of the points your paper made was that if you were not immune suppressed, then you didn't really have to worry about AIDS.

Ziegler: That wasn't even a tertiary concern of ours. We were trying to guess at the scientific truth of the matter. I don't think that had anything to do with it, frankly. In retrospect, it was a very weak hypothesis, because it didn't explain the timing of the epidemic very well. My contribution to that hypothesis was really the Kaposi's part of it, and that I think has held up pretty well.

Hughes: Well, explain that part of it.

Ziegler: Well, the article that Jay and I wrote had two parts to it. One was Jay's idea that in fact you had to be immunosuppressed in order to get the virus in the first place.

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Ziegler: He proposed that a causative agent was also an opportunistic infection, and that you had to have a suppressed immune system already, and the virus would then prey on people who were already immunologically weakened.

Hughes: Why did he think that?

Ziegler: Well, I think just looking at the epidemiology and at the patient characteristics that we were seeing--but we were only seeing one small corner of the epidemic. We hadn't really picked up on the global situation which was emerging, because the cases in Africa were coming in late. There were just scattered reports here and there. It was kind of hard to put it all together.

His theory didn't exclude an agent; in fact, we were thinking that an infectious agent was most likely going to be found. But I think his idea was that in order for the agent to take hold, you had to be immunosuppressed to start with. And there is still some evidence that that may well be the case. Certainly in hemophiliacs and others, there is sort of synergism between being infected and having a weakened immune system.

The Etiology of Kaposi's Sarcoma

Theory: Kaposi's as a Reactive Hyperplasia

Ziegler: But my contribution was more for the Kaposi's sarcoma, because we were interested in why Kaposi's should appear in these patients. We believed that it was sort of a reactive hyperplasia that then went on to become malignant, and that it was biologically very responsive to immune signals and probably cytokines and other wound-healing kinds of events that were going on, that it was almost like an endocrine tumor that would wax and wane in response to certain biologicals.

Hughes: Now, was this theory based on your own research?

Ziegler: This was based on the work I had done on Kaposi's in Uganda. I had been thinking about it for quite some time, and then trying to figure out how to explain the biology of the disease. The role of the immunosuppression was really what we set out to explain. Jay was much more the virologist of the two of us, and I was more interested in the cancer side. So that article simply proposed that Kaposi's was like a reactive hyperplasia that was hormone-responsive or responsive to other cytokines.

And I think that's been borne out by Gallo's work and others, who showed there are many cytokines which can make Kaposi's sarcoma cells grow. We tried in vain for years to get Kaposi's growing in tissue culture, and failed. It was Gallo's lab that succeeded simply because they were using conditioned

media from HIV-infected cells. They produce something in the media that stimulates Kaposi's to grow.

Hughes: Well, go back to the KS Clinic. Could you follow a patient through from the time he first presented?

Ziegler: Actually, the main proponent of the KS Clinic was Marcus Conant, because they were mostly his private practice clinic patients--they were coming to him for Kaposi's sarcoma. Later on, we were instrumental in setting up the Adult Immunodeficiency Clinic [at UCSF] which Harry Hollander now runs. In those days they were all coming through Marcus' clinic. Paul [Volberding] had a clinic down at the San Francisco General, and I saw patients here at the VA in the hematology-oncology clinic, and eventually we developed an AIDS clinic there as well. So we had three clinics, and we would come together and share our patient stories and try and make sense of this as time went on.

Donald Abrams, in the meantime, was collecting a large group of gay men who had lymphadenopathy syndrome, we called it. They were just coming to him with nonspecific symptoms and fever, and not feeling so hot, and weight loss, and night sweats, and these large lymph nodes. Donald started collecting cases, and he very soon collected several hundred, and wrote this up finally in the Annals of Internal Medicine.[1] But we would get reports of his group and his analysis.

An Hypothesis Associating Kaposi's Sarcoma and Volcanic Soils

Hughes: Is there still not anything definitive known about etiology?

Ziegler: No. Kaposi's is really an interesting mystery. Before you go, I'll give you a paper that was in the Lancet about two months ago.[2]

I explained to you that Kaposi's is one of these diseases that comes up with immunosuppression. Well, when we were in

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[1] D. I. Abrams, B. J. Lewis, et al. Persistent diffuse lymphadenopathy in homosexual men: Endpoint or prodrome? Annals of Internal Medicine 1984, 100:801-808.

[2] J. L. Ziegler. Hypothesis: Endemic Kaposi's sarcoma in Africa and local volcanic soils. Lancet, November 27, 1993, 342(8883):1348-1351.

Africa, we postulated that actually way back in 1967, not even knowing that this was going to be a disease that was excessively seen in immunosuppressed people. We did immunologic studies on patients in Africa, fully expecting to find impaired immunity. Not so; they were fine; they had good cell-mediated immunity; they had good humoral immunity. We couldn't find any immune defect in patients, but we were looking in the African patients at general systemic immunity. And then there was their ability totally to fight infection. And that was maybe self-evident; they didn't get opportunistic infections; they weren't ill from cryptococcal meningitis or any of these other things. They were perfectly healthy people. They just had Kaposi's sarcoma.

So we could not for the life of us link the African Kaposi's with immune suppression. And that's puzzled me for years; I've never been able to figure out why it is. Because everywhere else you find Kaposi's, for example, the classical Kaposi's in Europe, it's almost always in very old people--

Hughes: Where you get a natural decline in immunity.

Ziegler: A natural decline, exactly. And these Africans were young, robust peasants. These were farmers out in the fields.

This is a digression, but I think you'll find it interesting. Last year, I spent the year on sabbatical at Cambridge University, where my wife is doing some graduate work. I was puzzling about Kaposi's sarcoma and working on a grant that I hope will come through from the CDC to study this in Africa. In my research, I've been trying to explain why Kaposi's in Africa is so common there, and why it was not associated with immune suppression. Those were anomalies of the disease that never could be explained. You don't see it in South America; you don't see it in India; you don't see it in Asia or in Eskimos. But in certain parts of Africa, for example, in Rwanda, Kaposi's sarcoma is almost 20 percent of the adult malignancies. Just indigenous. Now, of course, with AIDS, in many countries it's 50 percent. Half of the tumors are Kaposi's sarcoma. But even before AIDS, it was very common, and I couldn't figure it out.

I was riding on the train from Cambridge to King's Cross [Station, London] with a colleague of mine, John Rickens, who's just one of these brilliant Cambridgian types, who's a great lateral thinker. I was showing him the maps. I said, "What on earth could this be? What explains these distributions?" He said, "Well, have you thought about the soil?" I said, "Yes, but the soil all through Africa is pretty much the same. It's just all laterite."

He said, "Well, there is a chap named Ernest Price who worked in Ethiopia, and he discovered a relationship between soil and elephantiasis." Elephantiasis in Africa has always been ascribed to filaria, a small worm that gets into the lymphatics and blocks them up. Price apparently found elephantiasis in the highlands of Ethiopia, where there are no filaria, but he was finding many, many villagers coming in with these huge, swollen limbs. He traced it to soil which is of a very fine consistency, like kaolin, like Kaopectate. It's clay soil with very slippery, very tiny colloidal particles.

When Price began to study this, he realized that the people who have elephantiasis live in areas where this kind of clay soil is really common. In fact, they are all peasants. They all work in the fields, and they stand in this soil up to their knees, and then they get swollen legs, which also are burning and itching and quite uncomfortable. If you put shoes on them and take them out of the soil, protect them from it, the swelling generally goes down and they're better again.

So he spent a lifetime studying this disease. He ended up calling it podoconiosis--there's a connection; I'll get to it in a minute. Podoconiosis he explained as follows: these peasants work in this soil with this particular consistency. They are heavily exposed in the lower extremities to these tiny clay particles. Clay particles get into the skin, under the skin, and enter the lymphatics, and cause fibrosis of the lymphatics and block them.

Price did enough epidemiology to convince many people that this was true. He found particles of silica, of aluminosilicates, in the skin and in the lymph nodes. He was able to reproduce the disease in rabbits by injecting aluminosilicates into their foot pads. He was able to find trace minerals in the tissues of these patients. Perhaps the most convincing thing was that he would sit in marketplaces with his wife--this is a very eccentric Englishman--and he and his wife would sit down there at knee level and count swollen legs of people who came in and out of marketplaces. They did it in many different marketplaces in different parts of southern Ethiopia.

In the areas where these clay soils were dominant, they had a 5 percent prevalence of swollen legs in the marketplace. In an adjacent area where it's sandy soil or loam soil, totally different consistencies, virtually no cases. So then Price said, "Well, elephantiasis really isn't a filarial disease; it's a soil disease." And he went around to different parts of Africa and began to find more cases. Every time he found cases, he found this kind of kaolin clay soil.

Well, where did he find it? He found it in Rwanda, Burundi, western Uganda. He found it in Ethiopia, in parts of Kenya, in parts of Tanzania. He linked it to volcanoes, and the reason he linked it to volcanoes was that the volcanoes in these areas produce a basalt which comprises the underlying rock. The soil that forms on top of this basalt is very likely to be kaolin and montmorillonite, very sticky soils, as opposed to the sandy soils that are more characteristic of the desert areas. These volcanic clay soils characterize the areas where he found elephantiasis throughout Africa.

And the most extraordinary thing, Price jumped across the whole continent of Africa to northwest Cameroon--that's the place where the lake exploded about five, seven years ago, and all that CO_2 gas killed all those villagers. Well, that's a very heavily volcanic area. In fact, a whole line of volcanoes runs straight into the continent there. And sure enough, what did he find? A lot of podoconiosis, elephantiasis, in that volcanic area. Now then he had to explain, well, there are volcanoes all over the world, why is it these African volcanoes are different? And he could never explain that. I think the best explanation is that the chemistry of the magma in these volcanic regions is quite different from the chemistry of the magma in the Pacific islands, like Hawaii and Japan, and along the continental volcanoes such as Iceland, and there's volcanic activity in India and so forth. The African, especially the east and west rift sections of Africa, have a very alkaline basalt. It has to do with the relatively recent eruption of the magma and the geochemistry and weathering of the region.

Well, to get back to my train ride: This fellow [Rickens] said, "Look up this Price and see if there's some relationship between the distribution of KS and soil composition, because your map looks a little bit like podoconiosis." So I looked up everything Price had ever written. I then went to the FAO [Food and Agriculture Organization] soil maps; got them out. Then I realized I had to learn a little geochemistry, and had to learn about volcanoes and crustal contamination, and then soil formation and catenas (soil layers and weathering effects). I got about ten books and sat down to study this for about three months.

In the end, I was convinced that the Kaposi's and the podoconiosis occupy the same geographical territory. The most interesting part was this huge cluster of Kaposi's sarcoma in south Nigeria and northeastern Cameroon, sitting right on top of that volcano. Plus, when you look at it in its microepidemiology, you find that Kaposi's sarcoma in Kenya, for example, is not uniformly distributed across the country. It

clusters on the rainy side of Mount Kenya and on the rainy side of Mount Elgon. When you look in Tanzania, you find that it's not uniform across the country. Again, it's clustered near Mount Kilimanjaro and then down in the Irunga plateau, which is a very heavily volcanic area. The whole country of Malawi has a relatively high rate of Kaposi's, and that lies along the whole southern branch of the Rift Valley.

So putting all the geochemistry together, to make a long story short, I came up with a hypothesis that in fact Kaposi's sarcoma in Africa is related to clay soil exposure, and that the clay gets into the skin and somehow disrupts the skin immunity to make it susceptible to Kaposi's. When you think about it, 85 percent of the cases of African Kaposi's are on the feet or the legs, and of the other, 10 percent are on the hands. So it has something to do with hands and feet, and exposure of some kind.

It took me back to thinking, Well, if there's an infectious agent involved here, it could come primarily from the soil. I can't think of what it might be, because soil really harbors just bacteria and fungi, and if either of those things were involved in Kaposi's, we'd know it. We could see them under the microscope. And I worked around that for a long time, and did a lot of soil microbiology study, and I could not come with any microbe linked with the soil.

Then I discussed it with a very bright scientist in Britain named Robin Weiss, who does a lot of the work with HIV. He said, "Maybe the soil is simply causing immunosuppression." I thought, Wow. That's something we never test. We never tested if there is localized immunosuppression in the hands and the feet. We were examining systemic immunosuppression and couldn't find it. But what if there was some local immunosuppression?

Well, then it occurred to me, why not? The soil gets into these tissues. One of the best ways to kill macrophages in tissue culture is to dump in aluminosilicates, kaolin, diamond dust. Immunologists love the stuff because they can completely eradicate all their macrophages with this treatment.

So I came to the point of view that somehow the immunosuppressive part of Kaposi's in Africa has to do with immunosuppression of the hands and the feet, and that it probably comes from exposure to this very fine clay soil, which you can only find in certain parts of Africa.

Hughes: There's no way of actually testing that hypothesis?

Ziegler: Oh, yes. We've got several ideas of how to test it! First of all, you have to find out if the skin of the hands and feet is in fact immunosuppressed, and you can do that very easily by doing a tuberculin test--positive here, negative here. That would be the simple way to do it. Another way to test it would be to take the tissues from the feet and the hands and see if they contain aluminosilicates, like Price showed in the podoconiosis patients. Another way would be to actually find the homes of patients with a high prevalence of Kaposi's sarcoma, and test the soil in those areas. On a grid, also test soil where there's no cases of Kaposi's sarcoma, and compare the soil samples. I mean, there are plenty of epidemiologic things you could do, none of which have been done, so it's totally theoretical at the moment, but it has geographical plausibility.

I gave the paper in a talk to the Geological Society in London, and they thought it had geochemical plausibility. At least, nobody shouted it down. It's consistent right now with many of the observations.

Hughes: What do your oncologist colleagues think about it?

Ziegler: Oh, everybody thinks it's a good idea. Obviously, it needs to be tested. Nobody's been able to explain the Kaposi's in Africa. That's the curiosity. [tape interruption]

Hughes: Anything more you want to say on that subject?

Ziegler: No. [laughs]

More on Characterizing AIDS

A Gay Disease

Hughes: Well then, I'd like to go back to the earlier question of the framing of the disease, and what implications that had, because certainly in the two places where the epidemic hit first in this country--California and New York--it was for a while very much framed as a homosexual disease. What did that do to your thinking?

Ziegler: Well, we were very puzzled by the high predominance in gay men, and of course, all kinds of theories emerged having to do with amebiasis and multiple infections and sperm, and immunologic reactions to sperm, and all kinds of other curious hypotheses

that came out. I think when the other populations developed AIDS a little bit later, such as [cases associated with] blood transfusions, hemophilia, and IV drug abuse, it was clear that this was just one generic problem that in the end turned out to be a way that the virus could be very efficiently transmitted, and that was through rectal sex.

Hughes: As early as August 1981, there were a number of heterosexual cases reported.[1] Nothing much seems to have been done with that information. Was it because AIDS was seen as a gay disease?

Ziegler: Yes, and somebody wanted to call it GRID [gay-related immune deficiency]. Well, I guess that's one of the lessons of science history, and that is that you must treat anomalies with great respect, because they're usually the ones that give you the answers--just like the code-breakers in Britain. I'm currently reading about cryptoanalysis during the war at Bletchley Park. Their reliance on these oddities, the anomalies, gave them the words needed to break the code.

Hughes: You and other people relatively early on suspected that it had to be an infectious agent. What would have been the rationale, if it were an infectious agent of some kind, of confining it to one population?

Ziegler: Yes, we couldn't understand that. By then, the epidemiologists were telling us, Look, the ones who seem to be most susceptible to this disease are people who had rectal intercourse one way or another, who were recipients of rectal intercourse; they were the most likely to be ill. So there were some practices that suggested that trauma and possible sperm exposure, things like that, might predispose a person to AIDS. And we puzzled quite a lot over that, and couldn't quite reconcile it with the other hypotheses except to say that whatever the agent was, it gets into the bloodstream. And once it's in the bloodstream, it can be passed to other people and also to infants. Hepatitis was the best model.

Latency

Hughes: What about the evolution of thinking about the latency period?

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[1] S. M. Friedman, Y. M. Felman, et al. Follow-up on Kaposi's sarcoma and Pneumocystis pneumonia. Morbidity and Mortality Weekly Report 1981, 30, #33, 409-410 (August 28, 1981).

Ziegler: That was another problem. I didn't engage too much in that aspect, but it was obvious, I guess, that there was something that happened to the gay population in the late seventies, early eighties, that propelled this disease. And then only in hindsight did we recognize that the virus was around, but was spread very rapidly, and probably caused disease in a much more accelerated way in the early part of the epidemic than it does now.

Immunostimulation

Ziegler: Our explanation for that was that these patients were already very immunostimulated. Again, I guess more or less in hindsight, we always think of immunosuppression/immunostimulation as kind of an on/off toggle switch, which is dead wrong. In point of fact, what we should have known all along and which everybody is rediscovering is that when somebody is immunostimulated, it doesn't mean they have a strong immune system. In point of fact, their immune system is probably diverted from what it should be doing.

We learned that years ago when we were studying malaria in Africa. Malaria is a disease that causes a very massive stimulation of the immune system: Spleens get big, immunoglobulins go up, these patients are very turned on immunologically. But they're not necessarily healthier. In fact, they're very unhealthy. If you have someone with acute malaria and try to give him a tetanus shot, he won't develop antibodies. He just doesn't respond to vaccines. If somebody has bad malaria, he is more susceptible to getting bad pneumonia. If you have malaria and measles together in children, you've got a lethal combination--25 percent of them die of pneumonia.

So while we were thinking immune stimulation is a great thing, gets the system revved up and that sort of thing, it's totally wrong. A stimulated immune system causes a functional immune suppression.

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Ziegler: What Don Abrams was noticing in his men with lymphadenopathy syndrome were patients who were massively immunostimulated. If you take the lymph nodes out and slice them up, they are filled with lymphocytes. Well, you would have thought, "Great, lots of lymphocytes, lots of immunity." Wrong. Lots of lymphocytes, all stimulated, not doing their job. And in fact, by getting

stimulated, the lymphocytes were putting out all these cytokines and making people feel lousy, like they had the flu.

So that's sort of a sidebar, but it does help explain that we were kind of on the wrong track when we were talking about immunostimulation/immunosuppression. Basically, immunostimulation equals immunosuppression.

Risk Groups

Hughes: The CDC identified risk groups for AIDS, the famous "four H's"--homosexuals, hemophiliacs, Haitians, and heroin users. Was the creation of risk groups standard CDC epidemiological practice?

Ziegler: Well, yes. No matter what you're studying, there will be some groups at risk for disease and some groups which aren't. I think that the epidemiologists used the term "risk ratio" and so forth to try and characterize somebody who's going to get sick versus somebody who isn't. I think it became a natural epidemiological tool to use. Because the disease was so stigmatized anyway, it quickly stigmatized the risk groups, and then there were a lot of very unseemly jokes.

Hughes: It also, from a public education standpoint, may have diverted attention from the message that I should think the CDC would have been trying to get through, namely behavior, rather than just what risk group you happened to be in, determines risk. If you're a Haitian, that really is irrelevant; it's what you do as a Haitian that should count. The other side of the coin was, if you're not in a risk group, you are not at risk.

Ziegler: Well, I think you've found a real Achilles heel in the whole process, and I don't know where the problem arose. I'm not sure I would blame the CDC in any way. I think they tend to think in terms of risk groups anyway, because it's an epidemiologic tool.

Fears about Heterosexual AIDS

Ziegler: I'm wondering if it isn't also the press. The press and the media were trying to make sense of this at the same time, and the thing that was really sensational was not a gay person who gets AIDS, it's an actual straight person who gets it. I remember in '84, '85, one of these magazines featured some heterosexual

couple with their baby afflicted with AIDS, like this epidemic is coming right into your living room. I think it caused a tremendous sensation, just as much as Rock Hudson and the basketball player "Magic" Johnson getting HIV.

Hughes: There was another incident like that, concerning a pediatrician by the name of [James] Oleske--

Ziegler: Oleske, yes, sure.

Hughes: --who had been seeing pediatric AIDS cases, and came to the conclusion that AIDS could be transmitted through casual contact. [Anthony] Fauci wrote an accompanying editorial, and the combination of the two really raised anxieties.[1] Do you remember the time?

Ziegler: Yes, I do. I think there is a psychosocial side. There was a certain amount of comfort among middle class, straight people, thinking, This epidemic is not my problem. I'm not gay; I'm not hemophiliac; I'm not Haitian. Therefore, no problem. And that was a flawed message for sure. Of course, you don't want to panic the entire world, but you also want to be prudent. So I think that there were problems there.

Personal Risk

Hughes: Well, it leads me to a question. What were you thinking, before the isolation of the virus, about personal risk? What was going through your head when you were treating patients?

Ziegler: I think we knew that this was pretty much a sexually transmitted disease, and as long as you were a monogamous couple, you were not at risk.

Hughes: I guess you did up until December 1982, but then when you had that baby with transfusion AIDS, how else could the disease in that case be transmitted except through blood?

Ziegler: That's true. Paul and I and Marcus and the rest of us who were dealing with AIDS patients, when we found out this was an infectious agent, obviously we all got a little nervous because we thought, Well, we've been drawing blood from these people and

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[1] J. Oleske, A. Minnefore, et al. Immune deficiency in children. Journal of the American Medical Association 1983, 249:2345-2349.

so forth. Could we have gotten it? And there was a period of anxiety there, I suspect, when everybody who was dealing with AIDS patients wondered could they become infected by physical contact with patients.

Hughes: Did you change any of your procedures?

Ziegler: I had always been very cautious. I had never stuck myself. I think basically what we did here in the hospital eventually was go to universal [infection control] precautions, which was the prudent thing to do anyway.

Hughes: Were those the same pre- and post-epidemic?

Ziegler: No. Post-epidemic, the rules got much more stringent--gloves for drawing blood, masks for coughing patients, and things like that.

Hughes: Were you involved with the committee at San Francisco General which devised the first infection control guidelines for AIDS? An article was published in the New England Journal.[1]

Ziegler: Yes, that was Merle Sande's committee. I was involved peripherally in that, but I didn't sit on that committee. There were a lot of committees in those days, and all these committees made an impact, because they got the rules changed. It took a while; it usually does with committees.

AIDS Activities at the VA

Hughes: Were you seeing considerable numbers of AIDS patients at the VA?

Ziegler: Here at the VA, we started seeing more and more patients. By 1982, we had about several dozen all together. By 1984, we were up into the hundreds. Now we're way up, 800, 900, 1,000--I'm not sure.

Hughes: Was there anything that differentiated these patients from the ones at San Francsco General and UCSF?

Ziegler: No. Just the geography of the hospitals. We were a veterans' hospital, so we tend to see slightly older patients. Paul's

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[1] J. E. Conte, W. K. Hadley, et al. Infection-control guidelines for patients with the acquired immunodeficiency syndrome (AIDS). New England Journal of Medicine 1983, 309, #12:740-744.

hospital [San Francisco General] is very close to the Castro [District], so he was seeing many gay men. And then a number of IV drug abusers found their way into the VA.

Hughes: Well, tell me in more detail what was going on from the earliest days in terms of AIDS activities at the VA.

Ziegler: I guess I'd have to say for quite awhile I was pretty much the only person here who was interested in AIDS. I tried to get other people interested, and there was a little bit of investigative curiosity, but as the patients began to come in, I guess the infectious disease clinic was the one that started getting involved. There were two people there who were pretty alert. One was Ira Tager, and the other was Peter Jensen. Peter now runs the AIDS Clinic and is very active. They began to see, as I did, the Pneumocystis pneumonia, and those infections which were problematic.

Hughes: Did other physicians hesitate for reasons that we already discussed in regard to UCSF?

Ziegler: Yes, I think so. I've always wanted to study that, Sally. I always was curious why it was. I almost did a questionnaire, because I was curious why it was that more faculty scientists didn't get more interested in this disease sooner. I mean, here is just an extraordinary new illness. You don't very often encounter new diseases. This is sort of like [William] Osler trying to figure out what typhoid was at the turn of the century --just great opportunities. But there was really a disinterest or apathy, and some scientists really wanted to distance themselves. They just didn't want to have anything to do with it, didn't want to serve on this committee, didn't want to investigate or treat patients, and the like.

Anyway, the VA was slow, but I guess I did a lot of stirring up. I got the hospital director, Larry Foye, to send in a message to the Central Office saying, "Other VAs may be encountering these patients; pay attention; we should get some policies." And I served on a central committee [Steering Committee on AIDS, 1987-1989] to set up policy, which eventually created an AIDS office at the VA, and then they got their act together.

Hughes: How early was that?

Ziegler: About 1985.

Hughes: So not terribly early.

Ziegler: Not terribly early, no. The VA was slow to get its act together.

AIDS Clinical Research Center, UCSF

Funding for AIDS Research

Hughes: Were you having trouble getting the necessary resources that you needed?

Ziegler: Well, no, because what happened was that in those early years, Marcus got to [Willie] Brown and they set up the [Universitywide Task Force on AIDS], what they now call the Universitywide AIDS Research Program. And Merle Sande headed that. They immediately gave us a grant for the AIDS Clinical Research Center [at UCSF]. Marcus was the director of that grant for about a year or two, and then I took over from him in 1985. I remained the director right straight up to 1992.

Hughes: Why did Dr. Conant step down?

Ziegler: I never could understand that. I think he had a very, very busy practice. He was not a keen administrator. Running the practice, watching the budget, monitoring clinics, paying employees, doing a whole lot of managerial things, I think he just decided that he would rather spend his time with his patients. He was also then on a campaign to try to launch [AIDS] vaccine programs. He wanted to make sure that the vaccine developers were free of liability, so he was introducing legislation to cap liability for vaccine and things like that. So he had other projects.

So Rudi Schmid, who was the [UCSF] dean, asked me to direct the AIDS Clinical Research Center.

Hughes: Why did he choose you?

Ziegler: I think because I was probably, in the UC system, the most senior physician working on AIDS. Merle Sande and Paul were setting up a big program down at the General. There wasn't much going on at the Moffitt Hospital [at UCSF], except in a small way.

AIDS Patients at Moffitt Hospital

Hughes: Well, that brings up a question: Why bother with Moffitt at all? Why not refer AIDS patients to the General [SFGH], where there was already so much going on?

Ziegler: I think the General had its hands full, for one thing. The Moffitt already had patients going through the system. I don't think it was in any position to ship anybody--the General generally takes care of the indigent of San Francisco.

Hughes: But there had been exceptions made already, because Don Abrams' lymphadenopathy patients moved from Moffitt down to the General.

Ziegler: Yes. Well, that happened when Abrams went down to work with Paul, that's true. He took a lot of his patients with him. But I think that was a special circumstance, because Don was one of the few gay physicians who was really looking after such a large cohort of gay men, and I think they all just decided they would stick with him.[1]

Hughes: So what you're saying is that it was natural that there were two university institutions dealing with AIDS patients; it didn't make sense to have it all at the General?

Ziegler: We didn't think it was sensible at all to centralize it. In fact, I think the collegiality of the group was such that we could all call each other and communicate very freely without need for any kind of hierarchy.

Ziegler as Director

Ziegler: I think I was chosen because I had a lot of experience, and because I was pretty senior and I had already done a lot of administrative work. Paul was quite young and new at the time. Marcus was just overwhelmed with his practice and other things, and I think he just wanted out. And there was nobody else. I guess maybe another candidate might have been John Greenspan,

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[1] For more on this subject see the oral history conducted with Donald I. Abrams, M.D., in The AIDS Epidemic in San Francisco: The Medical Response, 1981-1984, Volume II, Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 1996. Hereafter, this series.

because he was doing a lot of the oral biology and discovered hairy leukoplakia.[1] He is the current director after I stepped down.

I had a lot of support from the administration here. Ralph Goldsmith, chief of staff, everybody said, "This would be wonderful for the VA. We'll bring you money; we'll give you an office; we'll give you space. You hire Susie Hedberg and Layne Ethington and you get started," so I set up the center here at the VA.

Hughes: And that all came through UARP?

Ziegler: The AIDS Clinical Research Center gets about a million dollars a year, and the center is still going strong. The program has gotten rave reviews every year. It really worked well. And the reason it did, I think, was, A, because of the collegiality of the group, which really has been together right all the way through--Paul, Marcus, John [Greenspan], Harry Hollander, and many others. B, we had a very good administrative network; and C, we had a good infrastructure that we were able to fund. So a portion of those funds went to help pay for the AIDS clinics at the UCSF hospitals.

We were also able to set aside some funds for quick turnaround research projects, pretty much like the very first grant we got. So people who had a good idea could submit their idea in an abbreviated form, have a peer review, and get some seed money right away to start to do whatever it was. They only had to wait six weeks maximum.

Hughes: My heavens.

Ziegler: So we were able to fund lots of programs. I think the most successful part of that enterprise was the fact that we could use the resources of the AIDS Clinical Research Center, which had ultimately quite a few components to it--you might have seen one of the annual reports. But we basically had a very large network of clinics and resources--the tissue bank, the serum bank, the computer center, we had a lot of people involved, and we were able to leverage funds.

But what we accomplished in this whole enterprise was the ability to leverage funds. Our investigators used seed money to do pilot studies, get data, and apply for grants. We leveraged

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[1] See the oral history in this series with John S. Greenspan, Ph.D.

maybe six or seven major centers in the UC area, NIH funded centers on IV drug abuse and AIDS, and the Oral AIDS Center was leveraged off of the ACRC start-up funds. The VA itself got a grant from the VA central office of half a million dollars a year for VA research, also facilitated by ACRC. So I figure that over the years, we must have leveraged $30 or $40 million of research funds from other granting organizations coming in to UCSF. It was a big success from that point of view.

We were also able to support neglected groups: the women got together, and Ruth Greenblatt and Diane Wara and others said, "Okay, we need a consortium for women, research for women with AIDS." So the AIDS Research Center gave them a $10,000 grant. They were able to get secretarial help, get that organized, so now that's a big going enterprise of its own. That was the sort of thing that I enjoyed doing most when I was directing that center.

Hughes: Have you stepped down now?

Ziegler: Yes, I stepped down in 1993. John Greenspan is running it now. Marcus ran it for two years, and we were sort of co-running it. I was on the executive committee, and we would meet periodically.

Founding the AIDS Clinical Research Centers [ACRCs]

Hughes: Why was the ACRC founded, in 1983?

Ziegler: Well, it got founded because Marcus went to [Willie] Brown to get funds from the legislature. So they set up this universitywide task force on AIDS [1983], put Merle Sande in charge, and then the task force said, "Well, how are we going to spend this money?" Merle and I talked, and others; we decided they would set up two AIDS centers, one in southern California, one in northern California. So UCLA got one and we got one. Later on, UC San Diego got added in, so there were three centers. These centers were going to be centers of excellence that would coordinate and facilitate AIDS research in these different areas.

And then each one developed its own personality based on what sort of leadership and guidance and needs it had. Ours took on infrastructure by helping the clinics, setting up the mini-grant program, helping to leverage the other grantees, and coordinating research. And recently, the ACRC has been very much involved in the community response as well.

Hughes: How is that manifested?

Community Outreach

Ziegler: Well, [laughs] back in '89, '90, [State Senator, who was State Assmeblyman at that time] Tom Hayden held hearings to ask how the university was responding to the community needs and AIDS. So taking the cue from that, we began to look into the community to see what more we could do to facilitate university-community liaison. There are many nonprofit organizations looking at the needs of AIDS patients. There was no clear link between the research enterprise and the nonprofits' activities--the Shanti Projects, the information services, and so forth.

We got diverted in 1990 because of the AIDS conference [Sixth International Conference on AIDS] we had to put on in San Francisco. But that experience taught us that community liaison was essential for getting things done. In 1991 we sponsored community forums to inform the community about our research program. We created a community advisory board attached to our AIDS center, and finally now at the ACRC we have a full-time community liaison staff advisor who does nothing but work between the university and the community.

Hughes: When did the community outreach start?

Ziegler: Well, it's been forming over the years. I guess I would say I started it formally in 1991, and now 1994, it's going full steam.

Adult Immunodeficiencies Clinic, UCSF

Hughes: Is the Adult Immunodeficiencies Clinic at UCSF the functional successor of the KS Clinic?

Ziegler: Yes. Marcus Conant started the KS Clinic, and then it began to include AIDS patients with other conditions. Marcus had his own private practice, and those patients who were not in his private practice eventually found their way to what we called the Adult Immunodeficiencies Clinic. That was founded by the AIDS Clinical Research Center with funds from the center, and run by Harry Hollander, who had just completed his chief residency at the VA. Dick Root, who was the head of medicine at the time, Merle Sande, I, and others sat down and said, "Let's start this clinic." The

AIDS Clinical Research Center put a large amount of funding in to get it started, and then the funding slowly declined as the clinic began to pay its way. Now it's a full-fledged, self-supporting clinic with a big staff and many clients.

Hughes: The name implies that it's not strictly an AIDS clinic.

Ziegler: Well, it's sort of a euphemism; I think it's 99 percent AIDS.

Hughes: Is that part of the UCSF history of not really wanting AIDS there?

Ziegler: Yes.

Hughes: Does it see other adult immunodeficiencies?

Ziegler: I suspect so, but I'm not sure there's anything that isn't AIDS. [laughs] I mean, it's an AIDS clinic. In Uganda, they call an AIDS clinic an immune suppressive syndrome clinic--ISS. They will not say the "A" word. So it's universal. People don't like the label.

Hughes: All right, let's stop.

Early Lymphoma Cases

[Interview 2: February 16, 1994] ##

Hughes: Dr. Ziegler, do you remember vividly your first AIDS patient?

Ziegler: Yes, I do. My first AIDS patient was a gentleman who came in with the typical early manifestations of AIDS, with oral candidiasis, fevers, lymphadenopathy, and just feeling pretty punk--no energy. And as we followed him along, he developed a very large lymph node in his neck, which we biopsied, and it turned out to be a Burkitt's lymphoma, which is one of my great interests. So we were quite astonished to find that lymphoma as a manifestation of what we were regarding in those days as some kind of gay syndrome of immunodeficiency, but cause unknown.

It seemed to remind us that we were dealing with an immunodeficiency disease. Lymphomas of that type are very common in Africa where I worked, but then very rarely do they appear in young people in this country, except when they become severely

immunosuppressed, as we know now through kidney transplant series and so forth.

Hughes: Which hadn't been clear prior to that?

Ziegler: Hadn't been described before that. In fact, when we started talking amongst ourselves--and I think one of the great virtues of our little consortium, our Kaposi's sarcoma clinic, was that we all got together practically every week and exchanged views. Pretty soon, it was clear that there were a few other cases of lymphoma in the San Francisco area that were occurring in gay men, something that we hadn't anticipated.

So a few of us got together, pooled our resources, and reported the first four cases of lymphoma as a kind of an outbreak. That appeared in Lancet in 1982,[1] and was one of the first reports. And then later, we accumulated a large series of patients from many different medical centers around the country, about ninety different cases, and that turned out to be the definitive example of lymphoma as a diagnosis of AIDS.[2] And based on that paper, the CDC changed their AIDS-defining conditions.

Problems with Chemo- and Radiotherapy

Hughes: What did you do for lymphoma patients such as these in the early days?

Ziegler: We obviously knew we were dealing with immunosuppressed people, and when we started giving them standard chemotherapy and standard radiation therapy, we got quite a surprise. They were very fragile. They did not do well with chemotherapy or radiation therapy. They got quite toxic. Their bone marrow reserves were very limited, and when they got chemotherapy, their white counts bottomed out, as we say. When they got radiation therapy to the mucosal areas, they got very bad mucositis. So we were clearly dealing with a group of people who were not normal hosts, and that tied our hands with respect to therapy. We had to back way off on the intensity of therapy.

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[1] J. L. Ziegler, W. L. Drew, et al. Outbreak of Burkitt's-like lymphoma in homosexual men. Lancet 1982, 2:631-633.

[2] J. L. Ziegler, J. A. Beckstead, et al. Non-Hodgkin's lymphoma in 90 homosexual men. New England Journal of Medicine 1984, 311:565-570.

Hughes: Wouldn't there have been a red flag in your mind when you knew you were dealing with immunosuppressed people, and you knew that radiation normally surpresses the immune response?

Ziegler: Well, there was no way to anticipate it, until the early experience. We wouldn't have guessed that these patients would have reacted to the chemotherapy in such a strong way. They just don't tolerate it.

Hughes: Oh, you're saying chemotherapy; I'm thinking of radiation therapy.

Ziegler: Well, even the radiation was pretty toxic, too. But chemotherapy in healthy individuals is pretty well tolerated, and some can be cured. But for these patients, you just couldn't get away with the standard doses. They were just too toxic.

Hughes: These were drugs that you had used with success on other forms of cancer?

Ziegler: Yes. Absolutely. KS and lymphoma both.

Hughes: Well then, when they didn't work, what did you do?

Treating Opportunistic Infections

Ziegler: Well, we began to realize that by the time people get lymphoma and some of these other bad tumors, they also have a lot of other problems as well. They were getting Pneumocystis pneumonia; they were getting Mycobacterium avium, the tuberculosis condition; they were getting cryptococcal meningitis. They were getting other opportunistic infections that were very seriously compromising their longevity. So we began to wonder if there were certain circumstances in which we shouldn't treat them at all, rather than really compromise them with chemotherapy and then watch them die of some other opportunistic infection.

So for a number of years, there was a debate about whether to treat, or if you were going to treat, how vigorously to treat. Nowadays, I think we would treat, because we've got effective ways of postponing some of those opportunistic infections with prophylactic therapy. But in the early days, we really didn't know what we were battling with.

Diagnostic Criteria

Hughes: What were the things that you were particularly looking for to diagnose AIDS, in those very early days?

Ziegler: In the early days, before even the word AIDS came out, we didn't give it a name. Somebody wanted to call it GRID [gay-related immune deficiency], and that didn't seem to sit right, because we knew it was not a totally gay-related disease; there were other people who were susceptible. I guess I strayed off the question.

Hughes: What criteria were you using for diagnosis?

Ziegler: Well, we saw two different syndromes early on. Don Abrams was following a group of men who had developed idiopathic lymphadenopathy, called lymphadenopathy syndrome. In fact, Don and I wrote an article for one of the very first textbooks on AIDS by DeVita, Hellman, and Rosenberg that described that lymphadenopathy syndrome,[1] and then Don subsequently published it.[2] But what we were dealing with there was of course the earliest manifestation of the AIDS epidemic, before individuals got bad opportunistic infections.

Then what we noticed was that, as time went on, these lymph nodes began to melt away, and then the patients started getting thin, feverish, and quite miserable. They lost a lot of weight, and they got very pale and fatigued. But we didn't have any strict criteria. I think Pneumocystis pneumonia, any opportunistic infection, and then Kaposi's sarcoma and the lymphomas were diagnostic for AIDS. By that time, the CDC had set up diagnostic criteria, and then as you know, when time went on, things got added to it. But we were following CDC.

Hughes: Were some of those criteria set up at the KS meeting in September 1981?

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[1] J. L. Ziegler, D. I. Abrams. The lymphadenopathy syndrome and AIDS. In: V. T. DeVita, S. Hellman, and S. Rosenberg. Acquired Immune Deficiency Syndrome. New York: McGraw-Hill, New York, 1985, pp. 223-234.

[2] D. I. Abrams, B. J. Lewis, et al. Persistent diffuse lymphadenopathy in homosexual men: Endpoint or prodrome? Annals of Internal Medicine 1984, 100:801-808.

Ziegler: No, I don't think so. I don't know when the CDC actually published their early criteria for the syndrome,[1] and they certainly didn't call it AIDS until I think we were well into 1982 somewhere. So when their first criteria were published, I think it had to do mainly with an acquired immune deficiency in gay men--I can't remember quite how they characterized it. But we used their criteria.

Epidemiology

Ziegler: The CDC people were out here all the time, of course. Jim Curran, Harold Jaffe, and Don Francis and their group were spending a lot of time in California trying to figure out what was going on in San Francisco and L.A.

Hughes: Looking strictly at the epidemiology?

Ziegler: Yes. They were very interested in what was the network, how were people passing the disease, was there a connection between the different people who developed these conditions, what was the connection.

Their early papers, I think, were really extremely good examples of fairly complex epidemiology, because there were a lot of cofactors here. For a while, everybody thought it might be hepatitis, for example. Some hepatitis B [virus] was found in lymphocytes, and the epidemiology behaved very much like hepatitis--sexually transmitted, parentally transmitted, and so forth. But you couldn't really believe that a liver virus was causing a profound immunodeficiency, but it seemed to be something like that. In fact, for a while, as you know, in the blood banks, hepatitis was a surrogate marker [for HIV], until they got hold of the [HIV] antibody.

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[1] CDC published the first case definition of AIDS in September, 1982: Update on acquired immune deficiency syndrome (AIDS)--United States. Morbidity and Mortality Weekly Report 1982, 31:507-514.

Virology

Hughes: Well, this sort of problem occurred with CMV [cytomegalovirus] as well, did it not? Both viruses, from my understanding, are very common in sexually active homosexuals.

Ziegler: Right.

Hughes: How does a virologist go about figuring out what actually is causing--[laughs]

Ziegler: With great difficulty, I would have to say! We had Larry Drew right here in San Francisco, who was very active in CMV research, and of course Jay Levy, who has done a tremendous amount in the AIDS epidemic. Jay was looking at Kaposi's sarcoma, thinking that some of the clues to identifying the AIDS virus might come from growing Kaposi's sarcoma cells. This may be one of the peculiarities of the disease.

As I mentoned earlier, Jay and I also believed at the time that you had to be immunosuppressed in order to get the disease in the first place.[1] In other words, that AIDS was like an opportunistic infection. To some extent that was right, but epidemiologically, it didn't fit with all the subsequent data.

The virologists I think had a heck of a time trying to figure it out. Jay was working on it, and Larry Drew, and Girish Vyas was interested in the hepatitis side of things. He had his own theories. In the '81-'82 era, there was a mad and somewhat confused scramble for an etiologic agent. Obviously, by that time it was clear that AIDS was caused by an infectious agent that was spreading from person to person. This agent had a very long incubation period, was predominantly sexually transmitted but could be transmitted by blood and through the birth canal, and just nobody had a clue what it might be. And then Luc Montagnier published his LAV paper, I think in November of '83, and I think that this discovery was the main breakthrough on the path to discovery of HIV.

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[1] J. A. Levy, J. L. Ziegler. Hypothesis: Acquired immunodeficiency syndrome is an opportunistic infection and Kaposi's sarcoma results from secondary immune stimulation. Lancet 1983, 2:78-81.

Early Theories about Etiology

Hughes: Were you yourself fixing on any particular virus?

Ziegler: No. I went back and looked over my slides once, and my notes at those Kaposi's Sarcoma [Clinic] Conferences, and we had all kinds of models. We used to have lunch afterwards and try and figure out what was going on; we had drawings on table napkins. There were basically two theories: One was a sort of concatenation theory, where everything seemed to be conspiring in these people to suppress their immune system. We thought this might be a cumulative effect of multiple exposures to sperm and to viruses and to hepatitis and CMV, and that was sort of a major immune overload. But nobody could really buy into that, including us, because it never happened historically, that you would get a whole lot of different agents conspiring at once in the same person. And then it certainly didn't explain why other people were getting AIDS from blood. So that theory quickly fizzled out.

Then we realized that there was something profoundly wrong with the immune system, that was obviously acquired from sexual and other exposures, and that it was predominantly attacking the T4 cells, the CD4 helper lymphocytes. Art Ammann had a lot to do with making that particular discovery. I would say by the spring of '82, everyone was pretty much convinced we were dealing with an infectious agent. CDC by that time had published their very nice homosexual network paper, showing that in Orange County-L.A., everybody was having sex with everybody else, and you could see the network drawing of these multiple sexual contacts.[1]

Hughes: Which indicated an infectious agent?

Ziegler: Presumably, yes, that there was something moving through that group in a very rapid fashion. And then the question was, just what was it? I think the thing that Montagnier did, which was correct, was to look at the lymph nodes. That seemed to be where the virus was going to be, rather than in the bloodstream, where as we know, it was very hard to find the virus.

Hughes: But that wasn't an obvious thing to do, was it?

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[1] S. Fannin, M. D. Gottlieb, et al. A cluster study of Kaposi's sarcoma and Pneumocystis carinii pneumonia among homosexual male residents of L.A. and Orange County. Morbidity and Mortality Weekly Report 1982, 31(23):305-307 (June 18, 1982).

Ziegler: Well, I guess in retrospect it should have been, because we by that time had pieced together the natural history, where people start getting lymphadenopathy, swollen lymph glands. And then after a while, the lymph glands begin to go away; then patients start getting very seriously immunosuppressed. And during that phase, they go from relatively mild opportunistic infections like thrush and herpes zoster to really serious, big-time opportunistic infections like cryptococcal disease and Pneumocystis and TB. We had begun to see that shift, so if you were going to go for a tissue, you should go for one of the lymph nodes.

Hughes: What about the technology? From what I know about the work in Gallo's lab, there were some technical problems growing the cell lines.[1]

Ziegler: Right. We actually sent material to Gallo. I attended a very interesting conference in April of 1982. In fact, it was the American Cancer Society's annual meet-the-press conference, so they invited people out to talk about what they were doing. They were interested in my observation about lymphoma.

So I was on the same panel with Bob Gallo, who was actually coming not to talk about AIDS at all, but about HTLV-I [human T-cell lymphotropic virus-I]. We met on a number of occasions, because I knew him from NIH; we go way back to early days. I was saying, "Bob, you know, your lab ought to get interested in AIDS. I bet you we're dealing with some kind of human lymphotropic virus here. It probably isn't HTLV-I." I think most people had figured out that HTLV-I antibodies and so forth weren't present in these patients. So it wasn't that virus, but I said, "Gosh, it could be a relative."

Hughes: Why would you think that?

Ziegler: Well, as I say, it was spring of '82, we were pretty convinced that it was a transmissible agent, that it was lymphotropic, that it was doing something to the CD4 cells, and that it was spreading from one person to another sexually. So it had some commonality with HTLV-I.

Hughes: Well, behaving like that in some ways, yes, but it was cytopathic where the others were--what's the term?

Ziegler: Oh, the HTLV-I was latent, you mean?

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[1] Robert Gallo. Virus Hunting: AIDS, Cancer, and the Human Retrovirus: A Story of Scientific Discovery. New York: Basic Books, 1991.

Hughes: No, I mean that it was tumorogenic; it caused a proliferation of cells. And this virus was doing the opposite.

Overstimulation of the Immune System

Ziegler: Well, not necessarily. What we were seeing in the beginning was a proliferation of lymph glands. It was lymphadenopathy syndrome. If you take out the lymph node and slice it up, it was filled with lymphocytes, huge, giant follicles. So these lymphocytes and these lymph nodes were really switched on. Something was stimulating them into overdrive.

One of the things we learned, as I told you, was that a lymph node in overdrive is not necessarily a good situation. You know, we always talk about lymphoid stimulation as being a good thing; we want to stimulate, rev up your lymphocytes so that they're all ready to fight infection. In point of fact, that's not the way the system works. This system works because the lymphocytes are quiescent, and they only wake up when there's an alien invader. If they're all in a state of nonspecific activity, then they don't recognize any aliens, because they're all pre-empted; they're all stimulated. In fact, the lymphocytes are turning out all these cytokines which make people feel lousy. So the whole idea of immunosuppression and immunostimulation needs to be defined. Stimulation is not necessarily a good thing. Immunodepression is not necessarily a bad thing, if you're talking about numbers of switched-on lymphocytes.

Hughes: Is it AIDS that has caused this conceptual reorientation?

Ziegler: I think so, yes. I think a lot of people were talking about that in the earlier days, and then [Anthony] Fauci emphasized it in some of his work, that in point of fact AIDS is a disease, at least in its earliest stages, of lymphostimulation, and lymphostimulation is a perfect hotbed for viral replication, and a very unsatisfactory way for people to ward off infections. So you get into a positive feedback here: You set up the patient for infections; he gets infections; the infections stimulate the lymphocytes; the lymphocytes, thus stimulated, make more virus; more virus kills more CD4 cells. So each time you get a stimulation-infection cycle, you've kind of notched yourself down the ladder, immunologically speaking.

Which probably explains as the disease progresses why the lymph glands eventually involute; they just die of exhaustion. When you do an autopsy on an advanced AIDS patient, you can

hardly find the lymph glands, because they're all atrophied and shrunken.

Hughes: And that was known very early on?

Ziegler: Yes, pretty much. Some of the autopsies showed that there were different stages. Most of the autopsies, you see, were done on patients who had been far advanced, so they couldn't find the lymph nodes in the autopsies. Whereas, the biopsies that were done in, say, Don Abrams' [lymphadenopathy] group, all showed lymphoid stimulation.

I think a lot of the credit goes to the group at Stanford for showing that. Ronald Dorfman, who's really one of the world-class lymphologists, first described what he called follicular lympholysis. He saw that these lymph nodes in the early stages were very, very densely packed--follicular hyperplasia, as they call it. As the disease progresses, it goes into what he calls folliculysis--the lymph nodes just completely dry up and involute.

Hughes: Which you don't see in other diseases?

Ziegler: No. That was the very first time that had ever been described as a progressive thing. And I think Ron Dorfman and another pathologist, Karl Racz from Germany, were the first really to do excellent lymph node dissections. And Harry Ioachim too, in New York. All three of them, and the group at NYU, began to show that this involution was clearly what was happening in the lymph nodes. So all the road signs pointed to lymph glands as the site of infection. All the epidemiology pointed to an infectious transmissible agent. And it was just, who was going to be the first to find the virus? Montagnier, I think, gets the credit for that.

Hughes: You talked about this AIDS network at UCSF, which included Mt. Zion. How closely did Larry Drew interact?

Ziegler: Larry Drew was very much a part of it, yes.

Hughes: And of course, you here at the VA, and San Francisco General. But what about physicians elsewhere? How regularly were you in touch?

Ziegler: As time went on, a couple of things drew the community together. First of all, Donald Abrams I think gets the mountain of credit for mobilizing the community of private practitioners [the County Community Consortium], because clearly a lot of the gay men who were getting AIDS were seeing private practitioners in the

community. I can't remember all their names, but Don Abrams was contacted by many of them, because he was gay himself, of course, and he began to see a much bigger pattern in the community.

We were all brought together, I think from a community standpoint, by Merv Silverman, [director of the San Francisco health department]. He formed a task force under Mayor [Dianne] Feinstein in those early days to mobilize the city's response to the epidemic. The first and most obvious thing that he wanted to do was to close all the bathhouses, and that makes a whole interesting political-medical story of its own, that you may or may not want.[1]

Hughes: But he didn't want to close the bathhouses at first.

Ziegler: Well, actually, I think, to credit him, he wanted to close the bathhouses when he realized that they were the seat of the highest likelihood of transmission of whatever the agent was. I think Dianne was less interested in closing the bathhouses because the gay men were saying, "Look, you can't legislate our sex lives. This is a liberal community. If legislation is needed, we'll take care of it ourselves, but don't start closing down our fun houses."

In the end, it went to the courts, and they had to decide whether the bathhouses created a public health hazard or not. So they sent undercover investigators into the bathhouses with pads and pencils, and they sat in there and they wrote down everything they saw. And then they brought it back, and they published this huge tome full of--really just gay pornography is what it was. It's all on record down here in the City Hall. In the end, the judge ruled yes, the bathhouses should be closed, and so they closed them and there was an immediate appeal, and a week later they opened. And that was the end of the bathhouse story, as far as I remember. Eventually, the bathhouses kind of withered away, or cleaned up their acts.

Mervyn Silverman's Medical Advisory Committee on AIDS

Hughes: Did you have any role in closing the baths?

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[1] See the oral history in this series with Mervyn F. Silverman, M.D.

Ziegler: Well, more or less as a consultant.[1] There were about a dozen of us sitting around the table scratching our heads. There were gay doctors from the community. There was one, Bob Bolan, who was very active, who had a huge practice. And then Donald and Paul and myself, and Merv, the epidemiologist George Rutherford was there, and Andrew Moss[2]. We were all trying to say, "Look, we don't know what's causing this, but obviously there's something moving very swiftly through the gay community. This is a lethal condition, and whatever steps should be taken to curb it should be taken."

Hughes: And what was the forum for this discussion?

Ziegler: This was Merv Silverman's AIDS task force. It was commissioned by the mayor. We met on about a biweekly basis for quite a long time.

Hughes: Were you in touch with physicians outside the Bay Area?

Ziegler: Obviously the epidemic was spreading to other parts of the Bay Area. Progress of AIDS [research] was slower on the peninsula, because Stanford was behind us in research initiatives. It was quite advanced at Highland Hospital [Oakland], in Sonoma [County], and up in the Russian River area, where a lot of gay men go for their holidays. So where you found gay communities in concentration, you found people having to deal with this disease in the early days of the epidemic. But it clearly was not concentrated [only] in the Castro [District of San Francisco].

AIDS in the Gay Community

Hughes: Why did the epidemic manifest itself in the gay community, when there's no biological reason why an infectious agent couldn't spread beyond the so-called risk groups?

Ziegler: Yes. Well, it's my understanding that the virus was probably introduced into San Francisco in the late seventies, probably some time after 1976, 1977, in there. Although I didn't live here at the time, it was my understanding that the whole era of

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[1] See, in the Appendix, Ziegler's declaration in support of a temporary restraining order to close the bathhouses, October 10, 1984.

[2] The AIDS series includes oral histories with all these individuals, except Rutherford.

the seventies, particularly the end of the seventies, was a period of massive influx of young gay men to the Bay Area because of the enormous permissiveness of sexual freedom. The Castro became alive with gay activities.

I remember interviewing a number of my patients, many of whom were very forthcoming about their sex lives. They would go into a bathhouse and have encounters with ten or twenty individuals, all anonymous, all in the dark. They had these grope rooms and orgy rooms, and an extraordinary number of practices in which there's really ample opportunity for transmission of just about every bodily fluid into every bodily orifice among these men, in repeated fashion, with multiple exchanges of partners.

It turned out in the end, with all of the epidemiology, that receptive anal intercourse was the worst, the most dangerous practice, because infected sperm landing in the traumatized rectum found a ready entrance into the bloodstream, and I think that's how most of the cases were transmitted. But there were probably many other routes as well. But it's very hard to tease out exactly which practice is the most risky, because many of these men did everything. It was hard to find someone who was just exclusively a receptive intercourse person, and somebody who was exclusively another--they just switched back and forth.

I think from the point of view of transmission, though, San Francisco, L.A., New York, probably some parts of Houston and Miami, were areas where this degree of homosexual promiscuity was totally permitted and occurred.

Physician Networks

Hughes: Were you in touch with investigators in each of those locations?

Ziegler: We knew a lot about what was going on in L.A. because with the AIDS Clinical Research centers [at UCLA, UCSF, and UC, San Diego], we could keep in touch with our colleagues in L.A. They pretty much were seeing exactly the same pattern. The epidemiology was a little different, because their gay men were spread out all over Orange County, whereas ours were all focused in the Castro.

I had colleagues in Houston whom I saw at meetings who were seeing quite a lot of AIDS in Houston. And then of course in New York, [Alvin] Friedman-Kien and Linda Laubenstein. I had known

all those people before because of various other common interests. When I wrote the lymphoma paper,[1] for example, I had known before many of these people [who contributed lymphoma cases] through the oncology circles--Linda Laubenstein in New York, Sandy Levine in L.A., Ben Koziner at Memorial [Hospital in New York], and so forth. So we already had a network. So when AIDS came in and all these lymphomas cropped up, the network just kind of went into action. Each institution pooled ninety lymphomas for publication.

Hughes: So the structure was already in place prior to the epidemic.

Ziegler: Yes. It was kind of a loose structure of oncologists who all knew each other; we knew each other's work.

Hughes: Do you think the same thing occurred in other specialties, for example dermatology?

Ziegler: Yes. Definitely dermatology was the other link. Al Friedman-Kien and Marcus Conant and their colleagues in L.A. all noticed the Kaposi's connection simultaneously.

Hughes: Were those informal networks the main way of transmitting information?

Ziegler: Pretty much. I think you'd have to get all that first hand from Marcus,[2] but I would have thought yes. They had known each other before the epidemic.

Hughes: You relied on the networks because publication takes a long time, and you were having to deal with patients now.

Ziegler: Yes. I'm sure Al [Friedman-Kien] and Marcus talked with each other many times on the phone, and then contacted other people, because when a dermatologist sees an excessive number of an unusual disease, they report it to each other.

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[1] J. L. Ziegler, J. A. Beckstead, et al. Non-Hodgkins lymphoma in 90 homosexual men. New England Journal of Medicine 1984, 311:565-570.

[2] See the oral history in this series with Marcus A. Conant, M.D.

Ziegler: We got a publication in Lancet I think in the summer of '82, which was that outbreak paper.[1] Then I went to work and got the ninety patients and that was sent in around February of '84, just before the virus was actually announced by Gallo in the spring of '84, but by that time, of course, it was clear from Montagnier and from others that we were dealing with a transmissible agent. So yes, there was a lot of networking going on.

Hughes: So oncologists in general were pretty much alerted to watch for lymphoma?

Ziegler: Yes.

Multidisciplinarity

Hughes: AIDS was a new disease. What did that allow you to do that was different from working in a well-established field?

Ziegler: I found it terribly challenging and interesting and exciting. Obviously it was a devastating clinical problem too, which needed solutions. But from the point of view of an academic investigator, it opened just huge avenues of research possibilities. And as you say, we were in completely new territory, and there has never been, except for maybe measles and a few other conditions, an acquired immunodeficiency of this degree.

We were tremendously puzzled by what was going on, and we started networking with other disciplines, because clearly this was a multidisciplinary problem. First of all, you were seeing it in adults and in children; it involved oncology; it involved infectious disease and opportunistic infections; it involved the immunologists, and particularly those who were dealing with congenital immunodeficiencies; it involved dermatology; and most importantly it involved the epidemiologists, because in those days, what we needed was someone to come in and say, "Here's a pattern; here's how we can study it; this is what we need to do." And they started establishing the cohorts, these very important groups of people that gave us the profile of the disease over time.

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[1] W. L. Drew, M. A. Conant, et al. Cytomegalovirus and Kaposi's sarcoma in young homosexual men. Lancet 1982, 2:125-127.

Ziegler: I found it a very exciting opportunity because of all these different disciplines all tuning in to the same problem. Virologists of course, like Jay, all did a lot of sharing of information and ideas. Everybody put in their contribution. It's sort of like the proverbial elephant: we described the piece we could understand. But bit by bit, we began to see the whole beast.

Hughes: Had you ever worked with a multidisciplinary team of this nature before?

Ziegler: Well, cancer is by its nature multidisciplinary. Cancer involves on the biological side, a lot of knowledge of enzymology and pharmacology and immunology, and from the clinical side, radiation and surgery and chemotherapy and hematology. So yes, I think I'd have to say, if there was one breakthrough in oncology in the last two decades, it's probably been the fact that it does draw all the disciplines together. In the days when I was in training, doctors of different disciplines didn't often talk to each other. The surgeons didn't talk to the radiologists. There was no such thing as chemotherapy, except in the back wards of some of the big hospitals. There was virtually no communication about cancer, least of all with the patient.

Now, it's a revolution. The patient is the most proactive person, and all the disciplines now meet together in tumor wards, and share their data. So yes, by nature, oncology was already multidisciplinary.

Hughes: Is it fair to conclude from this that oncology in a sense set a precedent for a multidisciplinary approach to AIDS?

Ziegler: Yes, I think oncology gets a lot of credit for doing that. People like Paul Volberding, who'd already finished his training in oncology, were well tuned in to organizing these kind of multidisciplinary groups, and engaging the virologists and immunologists. He got quite a lot of support for that in the end through grants and various other centers that were forthcoming.

AIDS in Africa

AIDS and Civil Unrest

Hughes: You said last time that information about what was happening in Africa in terms of AIDS came in only as time went on. Why was that?

Ziegler: Well, AIDS arrived late in Africa. I'm not exactly sure why. I think part of it had to do with the mobility of people across the continent--truck drivers--and also had to do with civil unrest in various countries. I think Uganda suffered the worst, because it had a major civil war. I think it's not surprising that the very earliest cases of AIDS in Africa appeared in Uganda and in Zambia.

Hughes: Is that Idi Amin's uprising in the early 1970s that you're talking about?

Ziegler: That's right. I left Uganda in 1972, when Idi Amin took over. Then there was a series of really brutal killings and almost tribal genocide under Amin's reign. The deposed president, whose name was [Apollo M.] Obote, was sheltered in Tanzania. The president of Tanzania, [Julius K.] Nyerere, had no love lost for Amin. So he mobilized the Tanzanian army under Obote's instigation to overthrow Amin. And it took quite a while to do that.

In the process, the Tanzanian army marched up around the west side of Lake Victoria, and on their way, of course, they consorted with many prostitutes who were coming east from Zaire. So a lot of the epidemiology centers on that movement of troops through a relatively pastoral, rural area, and the arrival of many prostitutes from eastern Zaire and Rwanda looking for business. And of course, there is a lot of trans-African traffic in that general area anyway.

So the way it looks, the epidemic was picked up by the Tanzanian army, brought into Uganda on the western side of Uganda, and the biggest-hit area was in fact where that army spent most of its time, which was in the so-called "Luwero Triangle" and Rakai district. That's the district which they always show on the TV--where old women and children are the only ones left in the village because everyone else has died of AIDS. But that's where there was much civil unrest and troop movement.

When the civil war reached Kampala, HIV went along with the soldiers. About five or six years later, up comes HIV, in those very areas. People began dying of what they called "slim" disease, which was just a name for wasting and tuberculosis and diarrhea and other manifestations of AIDS.

Hughes: Are the manifestations of AIDS different?

Ziegler: Different in Africa. The biggest problem in Africa has to do with TB, which comprises about half of the cases of AIDS, just garden-variety TB, not the M. [Mycobacterium] avium that is prevalent in the U.S. And a whole range of opportunistic infections--toxoplasmosis and cryptosporidiosis, the usual things, also affect Africans. What they call "slim" disease is a gradual, progressive wasting disease with diarrhea, where victims just get thin as skeletons, and then ultimately die. These are the main manifestations of AIDS in Africa, plus Kaposi's sarcoma.

Heterosexual Transmission

Hughes: In Africa, AIDS is a heterosexual disease, yet here it is usually not perceived that way.

Ziegler: In this country, there is clearly heterosexual transmission. But it seems to be quite unbalanced. It's much harder for women to give HIV to men than the other way around. Maybe at a ratio of about ten to one. So in the early stages of the heterosexual epidemic, you have a few women infected, with the men being relatively less infected by the women. But when men have a huge turnover of partners, this collection of women serves as a "point" source of infection, and as the epidemic progresses, eventually the men become infected. And then the men take it home and give it to their wives, or their next partner. So it's transmitted much more readily from men to women than from women to men, simply because, I think, it's partly a matter of topography. The area of exposed genital mucosa is totally different between the sexes.

Hughes: Was that true in the early days of the African epidemic?

Ziegler: I think it was true in the early days there too, but there were repositories of virus mainly in the bar girls and the prostitutes. And when they were tested for HIV, clearly the prevalence was much, much higher than in the general population. And in Nairobi, where a very good study was done on a lot of prostitutes, within three years the numbers went from 30 percent

to 90 percent--virtually every prostitute was infected by 1990. They also found in those days that genital sores and ulcers clearly were a risk factor. So obviously, any break in the genital mucosa increased the chances of both spreading it and getting it.

Recognizing a Global Epidemic

Hughes: As this information came in from Africa, did it change how you approached the disease here?

Ziegler: I think we were just becoming cognizant of the fact that this was a world-wide epidemic. What we were dealing with was a virus that was spreading predominantly by a sexual route, and secondarily by blood and maternal-child transmission. But primarily sexually. In Africa, it was heterosexual, and in the U.S. it was largely homosexual, but there was plenty of overlap.

How did it affect us? Well, I think the effect was delayed. I don't think people really paid attention to the AIDS problem in Africa until around 1984-'85, when it was clear that the epidemic was widespread and expanding. The problem was, what can you do about it in Africa, and what can you do to treat it, diagnose it, and so forth?

And that's really where the World Health Organization came in. They made a big effort to set up a global program in AIDS. Jonathan Mann, of course, is legendary for his work in setting that up. They went really worldwide, because there were obviously problems in Brazil, in Thailand, now in India and Burma. By 1985 the World Health Organization was getting into high gear to try to bring this epidemic under control.

Hughes: Did it reinforce in a sense what you already knew, that the problem was not confined to the so-called risk groups?

Ziegler: Yes. I think most definitely.

Physician Decisions Regarding Involvement in the Epidemic

Hughes: Well, going back to the UCSF scene, Dr. Conant said in his oral history, and I quote, "John"--meaning you--"was extremely

effective at bringing respectability to an epidemic that the university didn't want anything to do with."[1]

Ziegler: [laughs]

Hughes: How were you bringing respectability to the epidemic?

Ziegler: Oh, I don't know what he meant by that. I think basically what happened was that there was just a small group of us very interested in an epidemic that was really highly stigmatized. I think that there were some people who, while they recognized that this was a devastating medical problem, were very uncomfortable dealing with the homosexual community, dealing with a disease that has so much stigma attached to it. I think some people just found it not something they felt they could either deal with, or be associated with. For whatever reasons, they just stayed away.

I guess Marcus just meant that he and I were probably the most senior people in the academy, and I was a full professor in residence, and I had a long career in academic oncology.

It was hard in those days to get some of the card-carrying, best immunologists to give this disease some thought. Little by little, they came on board. Dan Stites was one of the first [immunologists] to really get involved, and Art Ammann.

More on AIDS Activities at the VA

Early Research and Clinical Work

Hughes: I read that a Kaposi's sarcoma follow-up clinic was founded at the VA as early as 1981.[2] Were you behind that?

Ziegler: Yes. Well, I did most of the AIDS work here until Ira Tager and Peter Jensen got involved in it in the mid-eighties. They are both trained in infectious disease. In fact, their predecessor was a retrovirologist named Ashley Haas. He was here in the first year of the AIDS epidemic. We used to meet and talk about

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[1] Oral history in this series with Marcus A. Conant, M.D., p. 162.

[2] Peter M. Elias, M.D., to all dermatology residents and staff and B. Bielan, R.N., October 12, 1981. Ziegler correspondence, AIDS History Project, Department of Special Collections, UC San Francisco Library.

it, because one of the things he thought about was, gosh, could this be a retrovirus? He worked in "slow viruses", and in fact wrote a very good paper on it after he left. But he went off to Minnesota in 1982, so we lost our only retrovirologist.

Hughes: Was it unusual to have an individual doing very specialized research at the VA?

Ziegler: Well, it's not unusual here, because we have really world-class investigators in every area. But he just happened to be a retrovirologist, which was extraordinary, and I guess if history had taken a slightly different turn, Ashley might have been the person to discover HIV.

Hughes: What made him think that it could be a retrovirus?

Ziegler: Because the disease looked exactly like what he was familiar with, the scrapie virus in sheep, and there's also a retrovirus in goats and horses, and all showing manifestations of immune deficiency and other disorders.

Hughes: The long latency--

Ziegler: Yes, long latency, the dementia, the immunodeficiency, all of those things were very common in these diseases caused by animal retroviruses.

AIDS Activities from 1985 On

Ziegler: But I don't think really much happened at the VA until we got the AIDS Clinical Research Center set up in '85 at UCSF. Once that was running and we had money available, then we started bringing people into the VA for AIDS activites. We hired Sandy Charles as a research nurse, got the clinic in better shape, and started registering AIDS cases. Ira Tager got quite interested in it, as the new chief of infectious disease, and he set up a larger AIDS registry, and then things started moving along at a little faster pace.

By 1988 we got very serious about AIDS investigation when we were awarded our AIDS VACARE grant, the VA Center for AIDS Research and Education, which I started with Martin Heyworth, who now runs it. That primarily is an investigative center. We have a very good track record now in new AIDS discoveries.

Seeing Patients

Hughes: In the early days, when it was pretty much you alone seeing AIDS patients at the VA, how did you deal with opportunistic infections? You presumably are not an expert on infectious disease. How did you handle patients with problems that really weren't in your territory?

Ziegler: Well, they were partly in my territory, insofar as a chemotherapist renders people immunodepressed with cytotoxins. So as a profession, we have to deal with opportunistic infections. In fact, a lot of the early cases of Pneumocystis pneumonia were seen in leukemia patients who were treated with prednisone. So I was pretty familiar with the opportunistic infections, and we just treated them as part of our daily oncologic experience. But HIV disease obviously began to involve many other specialties--pulmonary for PCP and the other infections, neurology for dementia, dermatology clinics for Kaposi's and other skin problems.

We started doing some clinical trials in Kaposi's here, trying to figure out what was going on. Paul Volberding and I did a couple of early trials.[1]

Hughes: What was the referral system? How did an AIDS patient actually come to appear in one clinic or another here?

Ziegler: In the VA, it was hit or miss until we formed the AIDS clinic in 1985. If they had cancer, they came to the oncology clinic; if they had infection, they would come to the infectious disease clinic.

Hughes: Referred by a community physician?

Ziegler: Many patients were either in the system or got referred in by community physicians when they turned out to be veterans, because veterans have more or less free care here. So, of course, our population was almost entirely male. It was generally the older males. So the VA lagged behind the rest of the city a little bit in its referral patterns for AIDS. We now have about 800 AIDS patients registered, but in the early days, there were maybe twenty, thirty, forty--not too many. Not nearly the number they

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[1] J. L. Ziegler, P. A. Volberding, L. Itri. 13-cis retinoic acid for Kaposi's sarcoma. Lancet 1984, 2:641; P. A. Volberding, D. I. Abrams, et al. Vinblastine therapy of Kaposi's sarcoma in AIDS. Annals of Internal Medicine 1985, 103:335-338.

were getting down at the General, for example, and in Marcus Conant's clinic.

Hughes: There were three clinics here, which I would think must have been seeing AIDS patients--the dermatology clinic, the oncology clinic, and the infectious disease clinic.

Ziegler: Primarily oncology. That's where I saw most of my patients, because I was already part of the oncology clinic. So we saw the Kaposi's, and the lymphadenopathy patients would come up there as well. Not that they had malignancy, but they knew we were interested in patients with enlarged lymph nodes.

Hughes: Who knew?

Ziegler: Well, the doctors around--it got around pretty quickly that we were interested in this problem, so patients would filter in from other clinics.

Laboratory Tests

Hughes: In those early days, what sorts of lab studies were you ordering?

Ziegler: You mean clinical lab studies?

Hughes: Yes.

Ziegler: Just the usual things. It was a little [while] before we could understand why the CD4 lymphocyte count was the critical count in HIV disease, so we would order just lymphocyte counts and blood counts and sort of fly by the seat of our pants, do some skin tests, see if they were positive, that sort of thing. But we didn't have any sophisticated lab studies at all, not until the CD4 count became available as a routine test.

Hughes: Did that hold you back?

Ziegler: Yes, I think so. It took a while to get set up. That was a very complicated affair--it involves flow cytometry and a big machine, a technician; it was an expensive procedure. So we didn't get set up for that until I guess '86, '87.

Hughes: You couldn't farm this work out to UCSF?

Ziegler: Yes, we did in the end, and sent blood over there. In fact, I used to drive it over there myself and deliver it, to Dan Stites'

lab [in the Department of Laboratory Medicine]. They were the first ones to run CD4 counts here. They were useful for getting the baseline counts and so forth.

The AIDS Specimen Bank, UCSF

Hughes: Well, that leads rather nicely into the tissue bank. You are given credit, and John Greenspan, for having the concept of establishing a tissue bank.

Ziegler: Yes, I think these ideas all developed spontaneously in the faculty dining room [at UCSF]. But we knew we were starting up with an epidemic. We didn't know what was going to turn out to be important, or not. We knew that we should start getting baseline data to get patients registered as AIDS cases, and we probably should store away some serum samples just in case it turned out to be something we'd want to go back and look at.

I had already had a lot of experience with tissue banking because of the work in Burkitt's lymphoma in Africa. We had a huge serum and tissue bank there, that's still extant at the NCI. So I had already learned how to bank serum.

We sought funds to do that from our very first grant from the NIH [Spring 1983], and we were awarded funds to do that. John Greenspan agreed to set up the bank.[1] Then from there on, all the credit goes to him. He did a fantastic job, and runs it like the Chase Manhattan [Bank]. Every sample is accounted for, there are rules for taking specimens out, and for collaborations, and feedback for the results of the studies. It's a beautifully run tissue bank.

Hughes: Are its contents available to any legitimate researcher anywhere?

Ziegler: Yes. He's written several articles about it,[2] and it's registered in the NIH repository of AIDS samples and so forth. I must say, he probably has generated about 200 papers out of those sera. For example, samples from one of the big epidemiology cohorts is being kept there, the huge cohort of gay men that's

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[1] For more on the tissue bank, see the oral history in this series with John S. Greenspan, Ph.D.

[2] See, for example: J. S. Greenspan, M. Conant, et al. The UCSF AIDS specimen bank. Laboratory Medicine 1991, 22(11):790-792.

being followed longitudinally [Warren Winkelstein's San Francisco Men's Health Study].[1] Well, if you wanted to go back and look at all those sera and test a hypothesis, they're all sitting there.

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Hughes: That is known nationally?

Ziegler: Oh, yes. I'm sure John can fill you in on all the details, because he keeps the records, and publishes an account.[2]

Hughes: Was there any particular reason that he took the tissue bank on?

Ziegler: I think you'd have to ask him. That came about working on the AIDS problem. He and Deb[orah Greenspan] had already, I think, identified the oral hairy leukoplakia, for which he is now credited as co-discoverer, and he was very keen to play a role in the epidemic. John then got his oral AIDS center started up [in the UCSF School of Dentistry] and became one of the great champions of AIDS research. I think all of the credit for the tissue bank, beyond the concept, goes to him. He really made it work.

Association with the Gay Community

A New Experience

Hughes: Had you had previous contacts with the gay community?

Ziegler: No.

Hughes: What did that experience mean to you professionally and personally?

Ziegler: Well, I had never really had very much to do with gay people in my professional life--or my personal life, for that matter. So it came as a big shock to me to find out this whole subculture.

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[1] For the history of the San Francisco Men's Health Study, see the oral history in this series with Warren Winkelstein, M.D., M.P.H.

[2] For an annual report, see, for example: J. S. Greenspan, P. A. Volberding. AIDS Clinical Research Center [ACRC]. November, 1993. [Available from ACRC, UCSF]

And of course, I didn't know anything about the gay community before I arrived in San Francisco, until the early cases came to my attention. I guess I learned everything by talking with patients and hearing their stories.

They were very forthcoming, very friendly, and really wonderful, intelligent, lovely people. I felt very badly for them because they were just suffering from this terrible epidemic. It never bothered me in any social way. I was never embarrassed or discriminatory in any way. I just took it in stride. I got very friendly with our patients.

My own secretary was a gay man, worked with me for five years and developed AIDS and died, so I had one relationship with a man whom I could see from health right straight through to the end. It's very sad; he really was a lovely, lovely person, and worked so hard.

Chairman, Sixth International Conference on AIDS, San Francisco, June 20-24, 1990

Hughes: What about in terms of politics? I'm thinking particularly of your role as an organizer of the Sixth International Conference on AIDS, where--I don't have to tell you--there was quite a lot of input from the gay activists.

Ziegler: Yes.

Hughes: Did that experience change your political views?

Ziegler: Yes, I would say it had a profound effect. The story is very simple: When I took on this job as conference chairman in 1987, we looked at the AIDS conferences as scientific gatherings for traditionally advancing knowledge in the field, never thinking really that patient involvement or people with the disease should or could or would want to be involved in the more esoteric, scientific aspects.

Well, the activists obviously changed the face of that conference. Our colleague Bob Wachter, who was our program director, should be totally credited with having his finger on the pulse of that whole social change. He wrote a book about the

AIDS conference which is a very good read.[1] He starts his book, truthfully enough, by saying that when we were first approached by the gay community, somebody said, "Look, cancel the conference, because George Bush is requiring people coming into the country to get HIV tested, and we can't have the conference in the United States."

Being part bureaucrat, I said, "That's ridiculous. We've made all these commitments. We've earmarked the finances. There's no way I'm going to cancel this conference." And then they said, "Well, if you can't cancel the conference, at least move it to another place outside the country." We said, "No, we've got these commitments."

And then the gay activists came to us with this great moral dilemma: How can we condone putting on a conference in a country that refuses to let the patients whom we are treating come to the country without major discriminatory acts? Well, that kind of hit me like a ton of bricks. I never really moralized about my role as the conference director, but it became very quickly apparent that we had to work hand in hand with the gay community and work through this whole politico-social problem. Of course, that whole story is told in Bob's book, and I don't have to tell how we did it.

But I think it changed me. In the end, when we joined hands with the AIDS activists and walked down Market Street, it was the first time in my life I had ever taken to the streets for any cause. And I must say, my heart was in it by that point. I really did believe that the government had done badly by these young men, that there was a homophobia and a stricture that was predominantly very right-wing, Bush-Helms mediated in government, and that it was holding up AIDS research, and had a negative, adverse effect on these people. And I could really identify with how strongly they felt about the issues.

The AIDS activists, I think, in turn, welcomed our participation and our partnership, because we really reached out to them and got them totally involved in the conference, put them on all the committees. They made important program decisions, and we negotiated everything with them right down to the last detail. And in return, I have to say they kept their bargain. They did not disrupt the conference until the very end. They did promise a little "tweak". We weren't going to get away with a huge conference like this in San Francisco without a word from

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[1] Robert M. Wachter, The Fragile Coalition: Scientists, Activists, and AIDS. New York: St. Martin's Press, 1991.

the gay community. But they were very disciplined throughout the conference. They went to all the sessions. It was a huge success as far as nonprofit groups were concerned. There was a real sense of community, I think, largely through Bob Wachter's work with the activists and his ability to renegotiate with them through this period.

And in the end, I must say that they won the day. I think they made their statement, and they are now a part of the landscape. So that's my story of the activists; a lot of subplots of course.

Hughes: Yes. It's a story that can go on for hours.

NCI (National Cancer Institute)

Hypothesis: Separate Agents for AIDS and Kaposi's Sarcoma

Hughes: I read of an NCI [National Cancer Institute] program called SEER [Surveillance, Epidemiology and End Results] which found that the incidence of KS prior to 1980 in various participating cities, San Francisco being one of them, was several times higher than in cities such as Atlanta and Denver where AIDS is relatively rare.[1] What does that mean?

Ziegler: There's a long story around KS and its epidemiology. But the short version is that most people think that KS is caused by an infectious agent, not HIV, but an agent that is passed along with it, and that these were really two independent epidemics, both following pretty much the pattern of advanced promiscuity in the homosexual community in the seventies. And in point of fact, the dermatologists, when they looked back and began to see that there were a fair number of patients in their gay practices who had Kaposi's sarcoma but who ended up not having HIV. And quite a number, twenty, thirty, forty maybe. So for a very rare tumor, that's a very high number of people in one risk group to develop a tumor.

So the feeling was that there was another agent, that it was being passed among gay men, that if you got it along with HIV, you got bad Kaposi's sarcoma, or you had a much higher risk of

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[1] Robert S. Root-Bernstein, Rethinking AIDS: The Tragic Cost of Premature Consensus. New York: The Free Press, 1993, p.81.

getting Kaposi's sarcoma, than if you just got it by itself. But if you got it by itself and you were a gay man, your risk was higher than the general population. So my guess is that that blip in the SEER data suggests that there was an agent in the seventies transmitting Kaposi's sarcoma among gay men in those endemic cities surveyed by SEER.

Hughes: An agent totally unconnected with HIV?

Ziegler: Totally unconnected, except when HIV accompanies it, it raises the risk quite substantially.

Hughes: Do we then say now that HIV is a cause of Kaposi's?

Ziegler: I think we have to say that HIV is a cofactor that amplifies the risk of getting KS. I guess the best analogy would be smoking and asbestos exposure. If you get asbestos exposure, your risk of lung cancer is not so high, except for certain kinds called mesothelioma. If you smoke, your risk of lung cancer is dramatically higher, depending on how long and how much you've smoked. If you smoke and have asbestos exposure, the risk goes up several hundred fold because of the interaction between the two. So I think what we're talking about is sort of an interaction phenomenon.

In other words, if you're a child in Africa and you're unfortunate [enough] to get malaria and measles at the same time, your likelihood of dying becomes very high, usually from pneumonia. So these are disease interactions, and I think the Kaposi-HIV is an example of that. I don't know for sure, because nobody's found the Kaposi agent.[1] I expect there's one out there.

Hughes: It's amazing, with all the intense work, that an agent has not been found.

Ziegler: Well, it's like Hodgkin's disease. People have thought for years Hodgkin's disease was caused by an infection, and Epstein-Barr virus got put up on the list, and maybe there are a few other viruses as candidates. No one has been able to pin it down yet, and we've had Hodgkin's around for a long time.

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[1] In 1995, a herpes virus, human hersvirus 8, was identified in KS tumor cells. See, for example, J. Ambroziak, J. Blackburn, et al. Herpesvirus-like sequences in HIV-infected and uninfected Karposi's Sarcoma patients. Science 1995, 268:582-582.

Early Grants for AIDS Activities

Hughes: You spoke last time of the $1.4 million NCI grant, which you believe was the first federal grant for AIDS. The American Cancer Society grant, which you received in November, 1981, was of course not a federal grant.

Ziegler: Yes. I suspect we got one of the very first AIDS grants from the NCI; that I guess was in 1983.

Hughes: Yes, spring 1983. Please tell me as specifically as you can how that money was spent.

Ziegler: It gave us the next leg up after the American Cancer Society money ran out. That was only $50,000 for one year [January 1, 1982-December 31, 1982].[1] By the end of that year it was clear we needed to continue the Kaposi clinic, we should start a serum bank, we should start an epidemiologic study, and we should provide some funds for various laboratories to go after the immunology and the virology of the disease.

I can't remember the exact details of the grant, because I think Paul Volberding was the principal investigator at the time, but we divvied it up and basically kept the Kaposi clinic going, started the serum bank, helped get Andrew Moss started with his gay men's cohort, which was a very important epidemiologic survey. Some money went to Jay [Levy], some went to Dan Stites's immunology group, and one or two others.

Hughes: Well, how was it decided who was going to be PI [principal investigator]? In this case, it was Volberding, and you were co-PI.

Ziegler: We never really worried about it. Paul and I just sort of traded things back and forth over the years, and weren't concerned about who got the credit for what. I think in those days, I had an established career, and I had already written my papers and won my prizes. Paul was on his ascendancy, and I thought it was important for him to get some investigative experience. So generally we worked it out as a kind of a trade-off. I think I ended up with the directorship of the AIDS Clinical Research Center and he ended up with the running of the grants. We just went back and forth, just like the conference. We were good

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[1] Marcus A. Conant to Assemblyman Art Agnos, January 20, 1983. (Marcus A. Conant Kaposi's Sarcoma Notebook, January-June, 1983. Conant's dermatology practice office, San Francisco.)

friends and also just really very collegial about our academic work. I can't remember a single time when we ever had a disagreement.

Hughes: Amazing.

Ziegler: Yes, it is. He was just great to work with, easygoing, very bright, very hardworking, very responsible.

Hughes: Where was Marcus Conant in all of this? He had an appointment at UCSF as Associate Clinical Professor, but he wasn't a straight down the line academic professor.

Ziegler: Yes.

Hughes: What difference, if any, did that make?

Ziegler: I think Marcus' career took a major shift when AIDS came along, and I think he had to make a big decision which way to go. He was obviously capable of managing and assimilating all of the molecular biology and virology and immunology that went along with AIDS, but I think his heart was in his private dermatology practice. I think really when push came to shove, what he really wanted to do was to take care of his patients and see them through the best possible outcome of therapy.

Because of his silver tongue and his charisma and his access, was able to become very politically important. He made contact with Sacramento; he testified many times; he went on a big crusade to get the state government to limit liability for vaccine development, and he did a lot of this important work behind the scenes. He just worked very hard for the politics of AIDS at every level, including national. He started the AIDS Clinical Research Center [1983], he ran it for a couple of years, and we all kind of worked together.[1] Then I saw his path veer off toward his major interest in his patients, and toward a political agenda that he felt strongly about. And he is very effective at what he does. He is really good. He didn't abandon the science; I'm sure he's still very current on what's going on, but he just felt that with his talents and his interest, that was the way to go.

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[1] See: Marcus A. Conant, Director. AIDS Clinical Research Center: Progress Report, 1983-1984. January 1985. (J. S. Greenspan papers. UCSF School of Dentistry, CN 92-0123, carton 3-92, folder: AIDS Specimen Bank Report 83/84.)

B-Cell Immunodeficiency in AIDS and Immunostimulation

Hughes: Well, say something about the 1984 paper in JAMA on B-cell deficiency, of which Art Ammann was prinicpal author.[1] Tell me how that ties in with T-cell deficiency, which was what most people were thinking about, and with your theory of activation of the immune system. [tape interruption while Dr. Ziegler reviews paper]

Ziegler: The immunology of AIDS in the early eighties was almost as big a mystery as it is now. There's still a long list of possible ways that HIV can cause immunodeficiency, and nobody really knows which is correct, or whether they all may be correct. But back then, we were worried about the B cell arm of immunity, particularly in children.

As a pediatrician, Art Ammann was worried about children's antibody responses. He found that the B cells were all switched on. They were as much activated as were the T cells. I think what Art describes in that paper and what we subsequently came to learn was that the whole immune system got stimulated, and as I say, preempted. It was unable to do its job because it was in a state of high alert. But all the cells were churning out useless antibodies. The way the immune system normally works, as I explained, is that it lies in wait, and when an alien comes in, then it specifically responds to that antigen. So all this nonspecific immunostimulation was doing no good. The system was kind of "spinning its wheels."

But I think that was one of the earliest findings that showed immunoactivation in AIDS. These patients had immune complexes, and they had high gamma globulin levels. But when you challenged them with an antigen, they couldn't make appropriate antibody. That's reminiscent of other conditions where there's a lot of immune stimulation, and you think the host is going to be in great shape because it's got big lymph nodes and lots of gamma globulin. It turns out they're not in great shape at all because the lymphocytes are preempted.

Hughes: And was that a new idea?

Ziegler: I think it was a relatively new idea at the time. I don't think we really appreciated how important it was with respect to HIV,

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[1] A. J. Ammann, G. Schiffman, et al. B-cell immunodeficiency in acquired immune deficiency syndrome. Journal of the American Medical Association 1984, 251, no.11:1447-1449.

because it turned out subsequently that HIV becomes very promiscuous, if you will, in lymphocytes that are already activated and producing this positive feedback. So the more activation, the more HIV replication you get. Now Anthony Fauci is showing slides showing that when the immune system drops, the activation goes up, and that these are reciprocal events which actually worsen the AIDS.

In the early days, we thought, Well, here we have an immune deficiency; maybe we should be stimulating the immune system. Some people were actually thinking about giving BCG [Bacille Calmette-Guerin] and some of these other old-fashioned immune stimulants. Just the wrong thing. In fact, the next year, Dan Stites and I wrote a paper suggesting that we should actually try immunosuppressives to calm down the immune system, to put it at rest.[1] There was a group in France headed by a chap named Jean-Marie Andrieu who actually did try cyclosporin treatment in French patients, and got quite interesting results. But he was very badly maligned at the time because, unfortunately, they made an announcement in the press before they had published their paper, and it got a big play in the newspapers, and AIDS investigators thought they were kind of crazy.

Actually, as it turns out, it was not a bad idea at all, and Anthony Fauci in his very latest paper in Nature last fall said, "Cyclosporin might be working." [laughter] So the unfortunate thing is that in the immunology of AIDS, you can find these very trendy things happening, rediscoveries of old pieces of evidence that make people take a fresh look at things. But I think from my vantage, immunostimulation is bad news. It probably is also good news for the virus, bad news for the host, and that's pretty much what that paper showed.

AIDS: An Autoimmune Disease

Hughes: In 1986, you and Dan Stites published a paper suggesting that AIDS is an autoimmune disease.[2]

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[1] J. L. Ziegler, D. P. Stites. Hypothesis: AIDS is an autoimmune disease directed at the immune system and triggered by a lymphotropic virus. Clinical Immunology and Immunopathology 1986, 41:305-313.

[2] Ibid.

Ziegler: Yes. HIV gains access to the immune system through a sort of lock-and-key arrangement. We were trying to figure out what the CD4 molecule--this is the marker of one of the lymphocytes--does under normal circumstances. Why is it there in the first place?

It turns out that it is a recognition molecule for linking lymphocytes with macrophages so they can read a new antigen. The new antigen comes into the body, it gets into macrophages, gets presented on the surface of the macrophage, and then each individual lymphocyte has its own kind of code. If it codes in to that new molecule, it latches on, with the help of the CD4 molecule, and it goes into an activation state, saying, "This is an alien protein and I'm going to get myself duplicated to fight it."

We postulated that the HIV must resemble the normal "ligand" for CD4. This turns out to be a class II molecule found on the surfaces of macrophages (and B cells). These "look-alikes" might confuse the immune system. For example, if the body was making antibodies to HIV, then those antibodies might cross-react with the macrophages. Likewise, there is such a thing as anti-antibodies, which might also cross-react with the CD4.

We reasoned in that paper that this so-called antigen mimicry might disrupt the main recognition apparatus of the immune system in such a way that the presence of alien invaders couldn't be transmitted to the immune system because of this blockade. Further, the MCH [major histo-compatibility complex] class II mimicry might trigger a "host versus host" response, an idea taken up by later workers.

Over the last six years, some supportive evidence suggests that "autoimmunity" is at least one mechanism by which HIV does its damage to the immune system. It gets a little more complicated, because since then, there has been some information about super-antigens that nonspecifically stimulate the lymphocytes, and then they just implode.

There are other theories that in fact HIV sort of becomes an alien molecule and creates a kind of a graft-versus-host disease within the body. We called it in our paper "host versus host." but there is a condition called graft versus host, where if you take immune cells from one person and put them into another, there is an immune reaction that takes place where one set of immune cells fights the other set. That seems to be what's happening in AIDS. You get the same thing: You get lymphadenopathy, you get immune stimulation, you get weakness, weight loss, all the symptoms.

So anyway, that hypothesis still gets quoted in most articles looking at the pathogenesis of AIDS, including Fauci's recent one. And I think it's on the list of potential reasons why the immune system fails.

Hughes: How was it received at the time?

Ziegler: I think the idea of autoimmunity was appealing, because a lot of autoimmune conditions are caused by what we know as antigen mimicry: Something gets into the body that is a look-alike. The body makes an immune response to it, and then pari passu begins to attack the other tissue antigens which resemble it. There are plenty of diseases that are caused by that mechanism. Therefore, it would seem logical that HIV, which is a virus carrying a molecule that looks like a MHC class II antigen, could in fact incite such a reaction. And I think there is some evidence that it does. I don't think it's the main cause of immunodeficiency, but I think it's probably one of the contributors.

AIDS Education

Hughes: What about AIDS education?

Ziegler: I was very interested in this aspect.[1] We've obviously had lots of audiences to educate--patients, doctors, nurses, general population, and so forth. I worked a lot in that over the years. We made a training video for house officers, which is often used. We produced pamphlets about safety, prevention, and housestaff training. We sat on committees [devising protocols for] universal precautions, training medical students, AIDS curriculum, et cetera. For two years [1988-1990], I was on the board of trustees of the Marin Community Foundation. I was their main AIDS man in Marin, and we held round-table forums and conferences that had to do with AIDS education in the community.

Hughes: Was there any hesitation or censorship of sexually explicit language?

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[1] Dr. Ziegler has been director since 1988 of the VA Center for AIDS Research and Education. He was also co-principal investigator [1986-1989], with Dr. L. Zegans, of the AIDS Professional Education Program, funded by the National Institute of Mental Health. From 1988-1994 he was associate investigator at the Center for AIDS Prevention Studies, UCSF, for the International Training Program in AIDS Epidemiology, funded by NIH.

Ziegler: Well, Marin's a pretty liberal place. The county had a very modest AIDS problem to start with. The epidemic has worsened over the years. But no, there wasn't very much censorship. There was a lot of community interest. So I did a lot of AIDS education, here at the VA, at UCSF, in the community, making videos and pamphlets and lecturing.

Alternative Therapy

Hughes: Do you care to comment on alternative therapies for AIDS?

Ziegler: Some are very interesting, although they are intuitive. Some of them are awfully flaky. You never know when an alternative therapy is going to turn up something positive. Rational therapy is only rational on the surface. Then you get very empirical as soon as you start looking a little deeper. But I've never discouraged patients from alternate therapy, as long as it does no harm, or doesn't interfere with a clinical trial or other treatments known to be helpful.

In those days, gosh, there was everything under the sun--huge, huge doses of vitamin C. There was a guy down on the peninsula who gave grams and grams of the stuff, which one of my patients took religiously. Vitamins, and nowadays I think antioxidants--a whole bunch of alternative treatments are out there.

The San Francisco Model of AIDS Care

Hughes: How do you define the San Francisco model of AIDS care?

Ziegler: I think that's basically Paul's bailiwick. The definition is the creation of a multidisciplinary clinic with comprehensive care for AIDS patients, and predominant management in the outpatient setting. The idea is to try to get everything done on an ambulatory basis so that people can stay out of hospitals as long as possible and have a good quality of life. Part of this is the involvement by the community NGOs [nongovernmental organizations]--Meals on Wheels, hospice, and the support groups that characterize the nonprofit organizations in San Francisco. I think these are just immensely impressive, the way those groups mobilized on a shoestring.

The Personal Impact of the Epidemic

Hughes: Do you think that the epidemic has changed the way you relate to your patients?

Ziegler: Oh, yes. I'm much more humble, I think. [laughs] I'd never been arrogant, but generally an academic comes to these problems with a sense that modern science has the power to overcome disease. Then you come face to face with a really intractable illness. This disease is truly a major challenge. There are small bits of progress here and there, and hopefully a vaccine or something else will come in the future. But right now, we are very limited in what we can do. So I think it's just a matter of humility in the face of the adversity of nature that keeps you honest in this business.

Hughes: Do you think of yourself as an AIDS physician?

Ziegler: Oh, not really. I think of myself as a physician first, and as an AIDS physician second. My own career has been very eclectic. I've done pediatrics, adult medicine, and general practice. I've done oncology, I've done AIDS, research, education--a little bit of everything. So I don't pigeonhole my professional life.

Hughes: Do you want to comment on how the epidemic has affected you personally?

Ziegler: Sure. I've learned a great deal about activism and what it can accomplish and what it can't. I've learned a lot about homosexual culture and the homosexual community, and the IV drug abusing culture and community, which I never knew and wouldn't have really known much about otherwise. I think I've changed my political views from conservative to a great deal more liberal than they ever were, simply on the basis of personal contact with people and watching the activists and what they can accomplish, and empathizing [with] how they feel as a community, because it's easy to identify with these young, well-educated people. This is not a marginalized group by any means.

What else? I guess it's made me a little more humane, as far as dealing with really dreadful illnesses are concerned. And I think the collegiality that has developed among people who are fighting the AIDS epidemic has been very rewarding for me personally. I have the highest regard for my professional colleagues, but we've also become in many ways personal friends, just being thrown together in this arena. And that, I think, has been a big plus. We all shared a lot of the same feelings and same motivations, too.

The Epidemic's Impact on Health Care and Research

Hughes: What has been the impact of the epidemic on the way health care delivery is structured in this country?

Ziegler: I suspect AIDS is one of the things that is propelling us towards this so-called health care reform. Another major public health catastrophe will really push us over the edge, but I think AIDS gave a big shove in that direction. The cost of taking care of otherwise healthy young people is becoming a major burden on the health care system, along with business as usual. People are still getting heart disease and cancer at the same rate. So it's had a big impact there.

The activism issue has made everybody sit up and take notice. I suspect we'll see more of that in other diseases. We're certainly seeing it more now in breast cancer, and in possibly other illnesses as well. Other impacts? Well, I think it's helped to do what medicine needs to do anyway, and that is to get more interdisciplinary networking. But it's also raised a very interesting and important ethical issue about whom doctors are obliged to treat, and I think reaffirms the Hippocratic Oath of helping people and not discriminating against patients because of whatever [disease] they might have. So I think there's been an ethical benefit.

I think the epidemic has been a real shot in the arm for research. Very often, research never ends up finding what it started out to find. There are always little side arms that come up and distract and attract, and many discoveries come unexpectedly anyway. So being able to put this much effort into a field in which there is now a huge body of knowledge of virology and immunology is going to have major good spinoffs in other directions. I'm sure a lot of people could make lists of good things that have happened in other fields. Borrowing AZT from cancer chemotherapy to use against the virus is a perfectly good example of how these fields interact. And I'm sure there will be plenty of discoveries in the AIDS field that will help other diseases as well.

Hughes: Do you have anything that you want to add or set straight?

Ziegler: I don't think so. You've got a very good interview program here. No, I don't think I could add anything.

Transcribed and Final Typed by Shannon Page
Editorial Assistance and Index by Celeste Newbrough

TAPE GUIDE--The AIDS Epidemic in San Francisco: The Medical Response, 1981-1984: Volume IV

Interviews with John L. Ziegler, M.D.

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.

[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 Medical Response 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.

Donald P. Francis, M.D., D.Sc.

Dr. Donald Francis is currently President of VaxGen, Inc., a company dedicated to developing a vaccine for HIV. In February of 1992 he retired after 20 years in the U.S. Public Disease AIDS Advisor to the State of California and Special Consultant to Mayor Art Agnos in San Francisco. In the latter capacity he served as the Chair of the Mayor's HIV Task Force. Dr. Francis is a third-generation California physician having done his undergraduate studies at the University of California at Berkeley. He received his M.D. from Northwestern University and his Doctor of Science from Harvard. Before beginning his work on AIDS, Dr. Francis was involved in epidemic control around the world. He worked for the World Health Organization eradicating smallpox from Sudan, India and Bangladesh. He was also on the front line of the cholera epidemic in Nigeria in the early 1970s and the developmental work on the hepatitis B vaccine, both in the United States and the People's Republic of China. He began his work on AIDS in 1981. He was one of the first scientists to suggest that AIDS was caused by an infectious agent. As director of CDC's AIDS Laboratory Activities, he worked closely with the Institut Pasteur to prove that HIV was the cause of AIDS. He was also one of the earliest scientists to realize the impact HIV would have on the United States and has been an indefatigable advocate for a logical public response. After retiring from CDC, Dr. Francis joined Genentech in 1993 to head up the clinical research of their candidate HIV vaccine. In 1995, he became a founder and President of VaxGen, Inc., a spin-off company which, in a developmental partnership with Genentech, intends to develop a world-wide vaccine for HIV.

CURRICULUM VITAE

Personal

Name:	**Donald Pinkston Francis, M.D., D.Sc.**
Home Address:	1565 Bellevue Ave. Hillsborough, CA 94010
Born:	October 24, 1942, Los Angeles, CA

Education

1960-1961	Biological Sciences, College of Marin, Kentfield, CA
1961-1964	Biological Sciences, University of California, Berkeley, CA
1964-1968	Medicine, Northwestern University, School of Medicine, Chicago, IL
1968	Doctor of Medicine
1969 - 1971	Pediatrics, Los Angeles County/University of Southern California Medical Center, Los Angeles, CA
1971-1973	Epidemiology, Epidemic Intelligence Service, Centers for Disease Control, Atlanta, GA
1975	Virology, Postdoctoral Fellowship, Harvard University, School of Public Health, Boston, MA
1975-1977	Infectious Disease, Infectious Disease Fellowship, Channing Laboratory, Harvard Medical School, Boston, MA
1976	Board Certified, Pediatrics
1976-1979	Doctoral Student, Harvard School of Public Health, Boston, MA
1979	Doctor of Science (Virology)

EXPERIENCE

July 1989-February 1992	Centers for Disease Control Regional AIDS Consultant, Region IX, United States Public Health Service, San Francisco, California (Retired 2/1/92)
August 1988- January 1992	Special Consultant on AIDS, to Mayor Art Agnos, City and County of San Francisco, San Francisco, California
July 1985-June 1989	Centers for Disease Control AIDS Advisor to the Department of Health Services, State of California, Berkeley, California
September 1983-June 1985	Assistant Director, Division of Viral Diseases, Centers for Disease Control Atlanta, Georgia
May 1983-June 1985	Coordinator, AIDS Laboratory Activities, Division of Viral Diseases, Centers for Disease Control, Atlanta, Georgia
July 1978-September1983	Assistant Director for Medical Science, Hepatitis and Viral Enteritis Division, Centers for Disease Control, Phoenix, Arizona
September 1976-November 1979	Doctoral Student in Microbiology, Department of Microbiology, Harvard School of Public Health, Boston, Massachusetts
January-September 1976	Postdoctoral Fellow in Microbiology, Department of Microbiology, Harvard School of Public Health, Boston, Massachusetts
July 1975-July 1977	Research Fellow in Pediatrics, Channing Laboratory of Infectious Disease, Harvard Medical School, Boston, Massachusetts
May-June 1975	Consultant ; WHO : Smallpox Eradication, Bangladesh
July 1974-June 1975	State Program Coordinator, WHO : Smallpox Eradication, Lucknow U.P., India
September 1973 - July 1974	Consultant; WHO : Smallpox Eradication, Bareilly, U.P., India
January-September 1973	Consultant; WHO : Smallpox Eradication, Khartoum, Sudan
July 1971-December 1972	Epidemic Intelligence Service Officer, Centers for Disease Control, assigned to Oregon State Health Division; Clinical Instructor of Pediatrics, University of Oregon (Official entry into the Public Health Service, CDC)
January-June 1971	State Epidemiologist, U.S. Agency for International Development, Centers for Disease Control, River's State, Nigeria
January-December 1970	Resident in Pediatrics, University of Southern California Medical Center, Los Angeles, California
January-December 1969	Intern in Pediatrics, University of Southern California Medical Center, Los Angeles, California
July-December 1968	Pediatric Fellow, Children's Bureau, Department of HEW, Punjab, India

Honors and Awards

1968	U.S. Children's Bureau, Pediatric Fellowship Abroad
1970	Pediatric Resident of the Year, LAC/USC Medical Center
1975	Honorary Fellow, Indian Society for Malaria and Other Communicable Diseases (for Smallpox Eradication)
1975-78	U.S. Public Health Service, Career Development Award
1977	Smallpox Eradication Certificate, World Health Organization/Government of India (for smallpox eradication)
1977	U.S. Public Health Service, Commendation Medal (for Smallpox Eradication)
1983	U.S. Public Health Service, Group Award (for hepatitis B vaccine efficacy studies)
1988	Board of Directors Award/Cable Car Award (for outstanding leadership in AIDS)
1989	Thomas Parin ' Award, Americans for Sound AIDS Policy (for outstanding work in AIDS)
1992	U.S. Public Health Service, Meritorious Service Award (for AIDS prevention efforts)
1992	Legislative Resolution of Commendation, California State Legislature
1994	CenterOne Red Ribbon Award (for leadership in the fight against AIDS)

Committee/Task Force Membership

1985-1988	California AIDS Task Force
1988-1988	California AIDS Leadership Committee (Co-chair, Education and Prevention Subcommittee)
1988-1991	San Francisco Mayor's HIV Task Force (Chairman)
1988-1992	California AIDS Budget Task Force
1989-1992	California Medical Society, AIDS Task Force (Consultant)
1988-1991	Department of Defense, Retroviral Diseases Peer Review Panel
1991	California Ryan White CARE, Working Group
1993	Centers for Disease Control, Advisory Committee on Prevention of HIV Infection (Consultant)

International AIDS Conference Committees

1985	1st International Conference, Program Committee
1986	2nd International Conference, International Advisory Committee
1989	5th International Conference, Program Committee
1990	6th International Conference, Program Committee

Testimony/Participant

1985-1992	California Legislative Committees, multiple appearances
1987	National Academy of Science, Development of Vaccines for AIDS (Participant)
1987	National Academy of Science, AIDS Oversight Committee (Correspondent)
1987	World Health Organization, AIDS Short-term Consultant, Sudan
1989	President's Commission on AIDS
1990	U.S. House of Representatives, Budget Committee
1990	National Commission on AIDS
1992	Los Angeles Commission on AIDS
1992	U.S. House of Representatives, Oversight Committee

Clinical - Faculty Appointments/Teaching

1971-1973 University of Oregon, School of Medicine

1987- Present University of California, San Francisco

1985-1992, Lecturer at:

Stanford University, Palo Alto, CA

UCSF School of Medicine, San Francisco, CA,

Hastings Law School, San Francisco, CA

University of California, Berkeley, CA

U.C. School of Public Health, Berkeley, CA

U.C. Santa Cruz, Santa Cruz, CA

Donald P. Francis, M.D., D.Sc.
Publications

Francis DP. *Insulating public health from extremist politics. Do we need boards of health? Am J Pubic Health 1994;84:720-1.*

Francis DP and *Singleton JA. Reporting HIV-1 infection through the provision of essential services. JAIDS 1993;6:285-6.*

Francis DP. *Toward a comprehensive HIV prevention program for the CDC and the nation. J Am Med Assn 1992;268:1444-47.*

Donald P. Francis, M.D., D.Sc.
Publications

Francis DP, Anderson RE, Gorman ME, Fenstersheib M, Padian NS, Kizer, KW, Conant MA. Targeting AIDS Prevention and Treatment Toward HIV-1 Infected Persons. JAMA 1989;262:2572-2576.

Francis DP, Margolis HS. Worldwide Elimination of Hepatitis B Transmission: We Have the Way, We need the Will. Letter to the Editor, JAMA 1989; 261:2400-2401.

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Francis DP, Kaslow RA. Prevention – General Considerations. Chapter 15, p251-253.

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Ascher, MA, Gallo D, Francis DP. Human Retroviruses. Diagnostic Procedures for Viral, Rickettsial and Chlamydial Infections. Chapter 31, p1113-1140. 6th Edition American Public Health Association 1989. Editors: Nathalie J. Schmidt, Richard W. Emmons.

Francis, DP. Prospects for the Future. AIDS Principles, Practices and Politics. Part XI, p564-569. Reference Edition, Hemisphere Publishing Corporation, 1989. Editors: Inge B. Corless, Mary Pittman-Lindemann.

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Kizer KW, Conant MA, Francis DP, Fraziear T. HIV Disease Prevention and Treatment; A Model for Local Planning. Western Journal of Medicine. 1988. Oct; 149;481-485

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Halsey NA; Reppert EJ; Margolis HS; Francis, DP; Fields HA. Intradermal hepatitis B vaccination in an abbreviate schedule. Vaccine (England) Dec 1986, 4(4)p228-32.

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Xu ZY; FrancisDP; Liu CB; Purcell RH; Duan SC; Chen RJ; Wen YM. Prevention of hepatitis B virus carriage of infants using HBV vaccine in Shanghai. Prelimary report of a randomized double-blind placebo-controlled trial. Chin Med J. Sep 1985, 98(9)p623-6.

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Alter MJ; Favero MS; Francis DP. Cost benefit for vaccination for hepatitis B in hemodialysis centers (letter). J Infect Dis Oct 1983, 148(4)p770-1.

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Francis DP; Hadler SC; Thompson SE; Maynard JE; Ostrow DG; Altman N; Braff EH; O'Malley P; Hawkins D; Judson FN; Penley K; Nylund T; Christie G; Meyers F; Moore JN Jr; Gardner A; Doto IL; Miller JH; Reynolds GH; Murphy BL; Schable CA; Clark BT; Curran JW; Redeker AG. The prevention of hepatitis B with vaccine. Report of the Centers for Disease Control multi-center efficacy trial among homosexual men. Ann Intern Med Sep 1982, 97(3)p362-6.

Francis DP; Favero MS; Maynard JE. Transmission of hepatitis B virus. Semin Liver Dis Feb 1981, 1(1)p27-32..

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Reingold AL; Kane MA; Murphy BL; Checko P; Francis DP; Maynard JE. Transmission of hepatitis B by an oral surgeon. J Infect Dis Feb 1982, 145(2)p262-8.

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Francis DP; Essex M; Cotter SM; Gutensohn N; Jakowski R; Hardy WD Jr. Epidemiologic association between virus-negative feline leukemia and the horizontally transmitted feline leukemia virus. Cancer Lett Mar 1981, 12(1-2)p37-42.

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Donald P. Francis, M.D., D.Sc.
Major Accomplishments
(Since joining the Public Health Service)

August 1988 - January 1992	Special Consultant on AIDS to Mayor Art Agnos, City and County of San Francisco, San Francisco, California. Chair the Mayor's HIV Task Force, a broadly-based group consisting of business , religious and health care professionals.
July 1985 - June 1989	AIDS Advisor - State of California, Department of Health Services, Berkeley, California. Consultant - WHO, Sudan (August 1987) Member of the California AIDS Leadership Commttee (July 1988 to present). Assisted the State of California in instituting one of the most advanced HIV-prevention programs.
May 1983 - June 1985	Assistant Director, Division of Viral Diseases and Coordinator, AIDS Laboratory Activities, Atlanta, Georgia. Established the CDC AIDS Laboratory which performed much of the early work etiologically ilnking the AIDS virus (HIV) with AIDS.
July 1978 - May 1983	Assistant Director, Hepatitis Laboratories Division, CDC, Phoenix, Arizona. Designed and completed a trial of the newly developed hepatitis B vaccine. Designed and coordinated the first placebo-controlled trial of HBV vaccine in newborn babies (collaboratively, with the People's Republic of China).
July 1985 - July 1979	Infectious Disease Fellow, Harvard Medical School, Virology Doctoral Student, Harvard School of Public Health. Completed fellowhip in infectious disease. Completed doctoral degree in virology (awarded in November of 1979), studying the transmission and outcome of feline leukemia virus.
October 1976 - December 1976	WHO Consultant, Sudan. Member of a four-man team investigating and controlling the first outbreak of African Hemorragic Fever (Ebola Virus)
May 1975 - June 1975	WHO Consultant, Smallpox Eradication Programme, Bangladesh. Helped design and implement the program for elimination of smallpox from Bangladesh.
July 1974 - March 1975	State Program Coordinator, WHO Smallpox Eradication Programme, Lucknow, India. Helped design and supervise the eradication of smallpox from the state of Uttar Pradesh, India.
October 1973 - June 1974	WHO Medical Officer, Smallpox Eradication Programme, Lucknow, India. Helped design and supervise the eradication of smallpox from Bareilly Division, Uttar Pradesh , India.
January 1973 - October 1973	WHO Medical Officer, Smallpox Eradication Programme, Khartoum, Sudan. Designed and directed a national surveillance/control program for smallpox in Sudan. Assured the absence of smallpox from Sudan.
July 1973	Completion of Epidemic Intelligence Service training program.
April 1971	Member of the CDC team, Yugoslavia. Termination of smallpox transmission in Kosovo Province, Yugoslavia.

MERLE A. SANDE

Curriculum vitae

BORN: September 2, 1939

CHILDREN:

Suzanne	1962	Eric	1970
Cathleen	1964	Sarah	1973

EDUCATION:

B.S.	Washington State University, Pullman, Washington 1957-1961
M.D.	University of Washington School of Medicine, Seattle, Washington, 1961-1965

PROFESSIONAL CAREER:

1965 - 1966	Intern in Medicine, The New York Hospital, New York, New York
1966 - 1968	Assistant Resident in Medicine, The New York Hospital, New York, New York.
1968 - 1969	Assistant Resident in Medicine (Infectious Diseases), The New York Hospital, New York, New York
1969 - 1971	Clinical Instructor in Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas
1971 - 1974	Assistant Professor of Medicine, University of Virginia School of Medicine, Division of Infectious Diseases, Charlottesville, Virginia
1974 - 1978	Associate Professor of Medicine, University of Virginia School of Medicine, Division of Infectious Diseases, Charlottesville, Virginia
1976 - 1978	Vice-Chairman of Medicine, University of Virginia School of Medicine, Charlottesville, Virginia
1978 - 1980	Professor of Internal Medicine, University of Virginia School of Medicine, Division of Infectious Diseases, Charlottesville, Virginia
1979	Acting Chairman of Medicine, University of Virginia School of Medicine, Charlottesville, Virginia
1980 - 1996	Professor of Medicine, University of California, San Francisco School of Medicine, San Francisco, California

M. Sande, MD
March 1997

PROFESSIONAL CAREER: (continued)

1980 - 1996	Vice-Chairman of Medicine, University of California, San Francisco School of Medicine, San Francisco, California
1980 - 1996	Chief of Medical Services, San Francisco General Hospital, San Francisco, California
1996 - present	Professor and Chairman, Department of Medicine, and the Clarence M. and Ruth N. Birrer Presidential Endowed Chair in Internal Medicine, University of Utah School of Medicine, Salt Lake City, Utah.

MILITARY SERVICE:

1969 - 1971	Captain, U.S. Air Force, Wilford Hall Lackland Air Force Base, San Antonio, Texas

BOARD CERTIFICATION:

1971	American Board of Internal Medicine
1974	Subspecialty of Infectious Diseases

EDITORIAL APPOINTMENTS:

1981 - 1983	*Infection and Immunity,* Editorial Board
1980 - present	*Antimicrobial Agents and Chemotherapy*, Editorial Board
1988 - present	*AIDS*, Editorial Board,
1988 - present	*Journal of Acquired Immune Deficiency Syndromes*, Editorial Board
1989 - present	*Journal of Infectious Diseases*, Editorial Board
1991 - present	*Infectious Diseases in Clinical Practice*, Editorial Board
1994 - present	*Bulletin of the New York Academy of Medicine: A Journal of Urban Health*, Editorial Board
1997 - present	*Drug Resistance Updates*, Editorial Board

PROFESSIONAL SOCIETY MEMBERSHIPS AND HONORS:

Albemarle County Medical Society
Alpha Omega Alpha
American Association for the Advancement of Science
American Clinical & Climatological Association
American College of Physicians, Fellow, Virginia Chapter, ACP, Secretary/Treasurer, 1975-1979
American Federation for Clinical Research
American Medical Writers award, 1995
American Society for Clinical Investigation (ASCI)
American Society of Internal Medicine
American Society for Microbiology
American Thoracic Society
Association of American Physicians (AAP)
Association of Professors of Medicine (APM)
California Academy of Medicine
California Society of Internal Medicine
Infectious Diseases Society of America ; Council member, October 1986 - October 1989; Chairman, AIDS Subcommittee; Vice President, October 1990 - 1991; President-Elect, October 1991 - 1992; President, October 1992 - 1993.
International AIDS Society
Medical Examiner, City of Charlottesville, County of Albemarle, Virginia
National Advisory Allergy & Infectious Diseases Council, Council member, 1 November 1987 - 31 October 1991
Pacific Inter-Urban Clinical Club
Phi Beta Kappa
Phi Kappa Phi
San Francisco Chapter of International Association of Business Communicators' 1987 Communications Leader Award
Society of Experimental Biology and Medicine
Southern Society for Clinical Investigation
The National Foundation for Infectious Diseases, Board of Directors, 1981 - 1982, 1996 -
Virginia Thoracic Society
Western Society for Clinical Research
Western Association of Physicians

COMMITTEES:

AIDS Advisory Board to Director of Public Health, City and County of San Francisco, Member, 1981 - 1995
AIDS Advisory Committee, Department of Health Services, State of California, Ex Officio member, December 1985 - 1995

COMMITTEES (continued)

AIDS Drug Advisory Committee, Department of Health Services, State of California, Member, 1991-1992

AIDS Leadership Committee of the Department of Health Services, State of California, Member, May 1988-October 1989; member, Education & Prevention Subcommittee

AIDS Task Force, National Foundation for Infectious Diseases, member, 1986 - 1990

American Board of Internal Medicine, Subspecialty Board on Infectious Diseases, Member, July 1992 - 1997

American Heart Association Council on Cardiovascular Disease in the Young, Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Member

Bay Area Infectious Diseases Society, President, September 1984-December 1986

Bowman Foundation, University of Virginia, Charlottesville, Virginia, Chairman, 1978 - present

Data and Safety Monitoring Board of the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Member, 01 July 1992 - 1996

IDSA/FDA Contract, Subcommittee on Guidelines for Meningitis, member, 1988 - 1990

Infection-control Advisory Committee to Director of California Department of Health Services, Member, 1988

Interscience Confence on Antimicrobial Agents and Chemotherapy, Program Committee, 1981-1985; Associate Member, December 1985 - December 1988; Liaison representative to ISC, 1985 - 1988; Hoechst-Roussel Award Committee, 1986 - 1990

Infectious Diseases Society of America, Council member, October 1986 - October 1989; Chairman, AIDS Subcommittee; Vice President, October 1990 - 1991; President-Elect, October 1991 - 1992; President, October 1992 - 1993

Infectious Diseases Subcommittee for the Medical Knowledge Self-Assessment Program VI, American College of Physicians, 1982 - 1983.

Inter-American Society for Chemotherapy, Member, 1986

International Society of Chemotherapy, Executive Committee, co-opted member, 1985 - 1989

Maxwell Finland 1993 Award, Member, Chairman's Committee, National Foundation for Infectious Diseases

Mayor Dianne Feinstein's AIDS Task Force, Chairman, 1984-1987

National Institute for Allergy and Infectious Disease, Data Monitoring and Safety Board, 1990-1996

San Francisco Medical Society AIDS Task Force, Consultant, 1985 - 1990

The National Foundation for Infectious Diseases, Board of Directors, 1981 - 1982

The United States Pharmacopeia on Infectious Disease Therapy, Drug Information Advisory Panel, 1980 - 1987

University of California, San Francisco AIDS Coordinating Council, Chairman, June 1988 - 1996

University of California, San Francisco Task Force on AIDS, Founding Chairman, 1982 - May 1988

University of California Systemwide Task Force on AIDS, Chairman, 1983 - June 1988

Veterans Administration Central Office, Career Development Committee, 1984 - 1986

COMMITTEES (continued)

Virginia Partners of the Americas, Executive Committee, 1976 - 1979
University of Utah Graduate Medical Education Committee, 1996 to present
University of Utah Health Sciences System Management Committee, 1996 to present
University of Utah Clinical Sciences Council, 1996 to present
University of Utah Medical Board, 1996 to present

ORIGINAL WORK

1. Kilbourn E, Christenson W, Sande MA: Antibody response in man to influenza virus neuramidase following influenza. J Rirol 2:761-62, 1968

2. Barondess J, Sande MA: Some changing aspects of aortic regurgitation: an autopsy study. Trans Am Clin Climatol Assoc 80:23-36, 1968; Arch Intern Med 124:600-05, 1969.

3. Sande MA, Levison M, Lucas D, Kay d: Bacteremia associated with cardiac catheterization. N Engl J Med 281:1104-06, 1969.

4. Sande MA, Alonso D, Smith J, Hook E: Left atrial tumor presenting with hemoptysis and pulmonary infiltrates. Am Rev Respir Dis 102: 258-63, 1970.

5. Sande MA, Kaye D: Evaluation of methods for determining antibacterial activity of serum and urine after colistimethate injection. Clin Pharmacol Ther 11:873-82, 1970.

6. Sande MA, Johnson WD Jr, Hook EW, Kay D: Sustained bacteremia in patients with prosthetic cardiac valves. N Engl J Med 286:1067-70, 1972

7. Shafig S. Sande MA, Curruthers R, Killip T, Milhorat A: Skeletal muscle in idiopathic cardiomyopathy. J Neurol Sci 15:303-20, 1972.

8. Merrill C, Gwaltney J, Hendley J, Sande MA: Rapid identification of pneumococci: Gram stain versus the Quellung reaction. N Engl J Med 288:510-12, 1973.

9. Sande MA, Overton JW: In vivo antagonism between gentamicin and chloramphenicol in neutropenic mice. J Infect Dis 128:247-50, 1973.

10. Rein MF, Westervelt FB, Sande MA: Pharmacodynamics of cefazolin in the presence of normal and impaired renal function. Antimicrob Agents Chemother 4:366-71, 1973.

11. Wenzel RP, Hendley JO, Sande MA, Gwaltney JM Jr: Revised (1972-73) bivalent influenza vaccine. Serum and nasal antibody responses to parenteral vaccination. J Am Med Assoc 226:435-38, 1973.

12. Ries KM, Cobbs GC, Gillenwater JY, Levison ME, Mandell GL, Sande MA, Kay D: Double-blind comparison of carbenicillin indanyl sodium ampicillin and cephalexin in treatment of urinary tract infection. Antimicrob Agents Chemother 4:593-96, 1973.

13. Rein MF, Sande MA: Osteomyelitis caused by concurrent infection with Mycobacterium tuberculosisand Blastomyces dermatitidis. Am Rev Respir Dis 109:286-89, 1974.

14. MacIlvwaine WA IV, Sande MA, Mandell GL: Penetration of antistaphylo/coccal antibiotics into the human eye. Am J Ophthalmol 77:589-92, 1974.

15. Graybill JR, Sande MA, Reinarz JA, Shapiro SR: Controlled penicillin anaphylaxis leading to desensitization. South Med J 67:62-64, 1974.

16. Sande MA, Irvin RG: Penicillin-aminoglycoside synergy in experimental Streptococcus viridans endocarditis. J Infect Dis 129:572-76, 1974.

17. Dacey RG, Sande MA: Effect of probenecid on cerebrospinal fluid concentrations of penicillin and cephalosporin derivatives. Antimicrob Agents Chemother 6:437-41, 1974.

18. Hook EW III, Sande MA: Role of the vegetation in experimental Streptococcus viridans endocarditis. Infect Immun 10:1433-38, 1974.

19. Sande MA, Johnson ML: Antimicrobial therapy of experimental endocarditis caused by Staphylococcus aureus. J Infect Dis 131:367-75, 1975.

20. Greenlee JE, Johnson WD, Campa JF, Adelman LS, Sande MA: Adult toxoplasmosis presenting as polymyositis and cerebellar ataxia. Ann Intern Med 82:367-71, 1975.

21. Sande MA, Mandell GL: Effect of rifampin on nasal carriage of Staphylococcus aureus. Antimicrob Agents Chemother 7:294-97, 1975.

22. Bolton WK, Sande MA, Normansell DE, Sturgill BC, Westervelt FB Jr.: Vevtriculojugular shunt nephritis with Corynebacterium bovis. Successful therapy with antibiotics. Am J Med 59:417-23, 1975.

23. Hendley JO, Sande MA, Stewart PM, Gwaltney JM Jr.: Speard of Streptococcus Pneumoniae in families. I. Carriage rates and distribution of types. J Infect Dis 132:55-61, 1975.

24. Gwaltney JM Jr., Sande MA, Austrian R., Hendley JO: Spread of Streptococcus pneumoniae in families. II. Relation of transfer of S. pneumoniae to incidence of colds and serum antibody. J Infect Dis 132:62-68, 1975.

25. Sande MA, Gadot F, Wenzel RP: Point source epidemic of Mycoplasma pneumoniae infection in a prosthodontics laboratory. Am Rv Respir Dis 112:213-17, 1975.

26. Guerrant RL, Moore RA, Sande MA: Toxigenic E. coli in infantile diarrhea in Brazil. N Engl J Med 293:567-73, 1975.

27. Utz JP, Sande MA, Garriques IL, Mandell GL, Warner JF, McGehee RF, Shadomy S: Combined amphotericin B flucytosine chemotherapy in human cryptococcosis. J Infect Dis 132:368-73, 1975.

28. Evans FO Jr, Sydnor JB, Moore WEC, Moore GR, Manwaring JL, Brill AH, Jackson RT, Hanna S, Skaar JS, Holdeman LV, Fitz-Hugh GS, Sande MA, Swaltney JM Jr: Sinusitis of the maxillary antrum. N Engl J Med 293:735-39, 1975.

29. Dilworth JA, Stewart P, Swaltney JM Jr, Hendley JO, Sande MA: Methods to improve detection of pneumococci in respiratory secretions. J Clin Microbiol 2:453-55, 1975.

30. Hood EW III, Roberts RB, Sande MA: Antimicrobial theraphy of experimental enterococcal endocarditis. Antimicrob Agents Chemother 8:564-70, 1975.

31. Joyce RA, Sande MA: Mechanisms of anaemia in experimental bacterial endocarditis: anaemia in experimental endocarditis. Scand J Haematol 15:306-11, 1975.

32. Strausbaugh LJ, Dilworth FA, Swaltney JM Jr., Sande MA: In vitro susceptibility studies with josamycin and erythromycin. Antimicob Agents Chemother 9:546-48, 1976.

33. Sande MA, Courtney KB: Nafcillin-gentamicin synergism in experimental staphylococcal endocarditis. J Lab Clin Med 88:118-24, 1976.

34. Wenzel RP, Hunting KJ, Osterman CA, Sande MA: Providencia stuartii hospital pathogen: potential factors for its emergence and transmission. Am J Epidemiol 104:170-80, 1976.

35. Minoro MR, Sande MA, Dilworth JA, Mandell GL: Cefamandole treatment of pulmonary infection caused by Gram-negative rods. J Antimicrob Chemother 2:49-53, 1976.

36. Sherertz RJ, Dacey R, Sande MA: Cefamandole in the therapy of experimental pneumococcal meningitis. J Antimicrob Chemother 2:159-65, 1976.

37. Strausbaugh LJ, Bolton WK, Dilworth JA, Guerrant RL, Sande MA: Comparative pharmacology of josamycin and erythomycin stearate. Antimicrob Agents Chemo 10:450-56, 1976.

38. Thompson RL, Sande MA, Wenzel RP, Hoke CH, Swaltney JM Jr.: Swine influenzae infection in civilians. Report of two cases. N Engl J Med 295:714-15, 1976.

39. Bodine JA, Strausbaugh LJ, Sande MA: Ampicillin and an ester in experimental Hemophilius influenzae meningitis. Clin Pharmacol Ther 20:727-32, 1976.

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41. Suratt PM, Swaltney JM Jr, Sande MA: A rapid method of disinfecting the bronchofiberscope. Am Rev Respir Dis 114:1198-2000, 1976.

42. Strausbaugh LJ, Mandaleris CD, Sande MA: Cefamandole and ampicillin therapy in experimental /haemophilus influenzae meningitis. J Infect Dis 135:210-16, 1977.

43. Strausbaugh LJ, Mandaleris CD, Sande MA: Comparison of four aminoglycoside antibiotics in the therapy of experimental E. coli meningitis. J Lab Clin Med 89:692-701, 1977.

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49. Strausbaugh LJ, Sande MA: Factors influencing the therapy of experimental Proteus mirabilis meningitis. J Infect Dis 137:251-60, 1978.

50. Korzeniowski OM, Wennersten C, Mollering RC Jr., Sande MA: Penicillin-netilmicin synergism against Streptococcus faecalis. Antimicrob Agents Chemother 13:430-34, 1978.

51. Scheld WM, Valone JA, Sande MA: Bacterial adherance in the pathogenesis of endocarditis: interaction of bacterial dextran, platelets and fibrin. J Clin Invest 61:1394-1404, 1978.

52. Calderone RA, Rotondo RJ, Sande MA: Candida albicans endocarditis: ultrastructural studies of vegetation formation. Infect Immun 20:279-289, 1978.

53. Sande MA, Sherertz RJ, Zak O, Strausbaugh LJ: Cephalosporin therapy of experimental meningitis. J Infect Dis 137 (Suppl): S161-68, 1978.

54. Gwaltney JM Jr, Sydnor T, Hamory B, Seale D, Sande MA: controlled trial of trimethoprim-sulfa in the treatment of acute maxillary sinusitis. Current Chemother 1:120-21, 1978.

55. Korzeniowski OM, Carvalho EM Jr., Rocha H, Sande MA: Evaluation of cefamandole therapy of patients with bacterial meningitis. J Infect Dis 137 (Suppl): S160-63, 1978.

56. Sande MA, Sherertz RJ, Zak O, Dacey RG, Bodine JA, Strausbaugh LJ: Factors influencing the penetration of antimicrobial agents into the cerebrospinal fluid of experimental animals. Scand J Infect Dis 14: (Suppl):S160-63, 1978.

57. De Carvalho EM, Filho, Costra E, Silva IC, Silva CP, Costa YA, Korzeniowski OM, Sande MA, Rocha H: Tratamento da meningite bacteriana com cefamandole. Published in Revista do Instituts de Medicina Tropical de Sao Paulo, 1978.

58. Scheld WM, Brown RS Jr, Sande MA: Comparison of netilmicin with gentamicin in the therapy of experimental E. coli meningitis. Antimicrob Agents Chemother 13:899-904, 1978.

59. Miller J, Sande MA, Gwaltney JM Jr, Hendley JO: Diagnosis of pneumococcal pneumonia by antigen detection of sputum. J Clin Microbiol 7:459-62, 1978.

60. Spyker DA, Thomas BL, Sande MA, Bolton WK: Pharmacokinetics of cefa/clor and cephalexin: dosage nomograms for impaired renal function. Antimicrob Agents Chemother 14:172-77, 1978.

61. Scheld WM, Royston D, Harding SA, Hess CE, Sande MA: Simultaneous disseminated aspergillosis and zygomycosis in a leukemic patient. South Med J 72:1325-28, 1979.

62. Harding SA, Scheld WM, Feldman PS, Sande MA: Pulmonary infection with capsule-deficient Cryptococcus neoformans. Virchows Arch [Pathol Anat] 382:113-18, 1979.

63. Scheld WM, Fletcher DD, Fink FN, Sande MA: Response to therapy in an experimental rabbit model of meningitis due to Listeria monocytogenes. J Infect Dis 140:287-94, 1979.

64. Scheld WM, Fink FN, Fletcher DD, Sande MA: Mecillinam-ampicillin synergism in experimental Enterobacteriaceae meningitis. Antimicrob Agents Chemother 16:271-76, 1979.

65. Harding SA, Scheld WM, McGowan MD, Kelley WJ, Sande MA: Enzyme-linked immunosorbent assay for detection of Streptococcus pneumoniae antigen in experimental meningitis. Trans Am Neurol Assoc 103:142-46, 1979.

66. Dacey RG, Welch JE, Scheld WM, Winn HR, Jane MA, Sande MA: Alterations of cerebrospinal fluid outflow resistance in experimental bacterial meningitis. Trans Am neurol Assoc 103:142-46, 1979.

67. Scheld WM, Thomas JH, Sande MA: Influence of preformed antibody on experimental Streptococcus sanguis endocarditis. Infect Immun 25:781-85, 1979.

68. Scheld WM, Park TS, Dacey RG, Jane JA, Winn HR, Sande MA: Clearance of bacteria from cerebrospinal fluid to blood in experimental meningitis. Infect Immum 24:102-05, 1979.

69. Hamory BH, Sande MA, Sydnor A Jr, Seale DL, Gwaltney JM Jr: Etiology and antimicrobial therapy of acute maxillary sinusitis. J Infect Dis 139:197-202, 1979.

70. Roberts TL III, Futrell JW, Sande MA: Antibiotic penetration into normal and inflamed tissues as reflected by peripheral lymph. Ann Surg 189:395-403, 1979.

71. Moellering RC, Korzeniowski OM, Sande MA, Wennersten CB: Species-specific resistance to antimicrobial synergism in Streptococcus faecium and Streptococcus faecalis. J Infect Dis 140:203-08, 1979.

72. Bennett JE, Dismukes WE, Dumas RJ, Medoff G, Sande MA, Gallis H, Leonard J, Fields BT, Bradshaw M, Haywood H, McGee ZA, Cate TR, Cobbs Cb, Warner JF, Alling DW: A comparison of amphotericin B alone and combined with flucytosine in the treatment of cryptococcal meningitis. N Engl J Med 302:126-31, 1979.

73. Rogers BH, Donowitz GR, Walker GK, Harding SA, Sande MA: Opportunistic pneumonia. A clinicopathologic study of five cases caused by an unidentified acid-fast bacterium. N Engl J Med 301:959-61, 1979.

74. Strausbaugh LJ, Murray TW, Sande MA: Comparative penetrations of six antibiotics into the cerebrospinal fluid of rabbits with experimental staphylococcal meningitis. J Antimicrob Chemother 6:363-71, 1980.

75. Scheld WM, Dacey RG, Winn HR, Welsh JE, Jane JA, Sande MA: Cerebrospinal fluid outflow resistance in rabbits with experimental meningitis. Alterations with penicillin and methylprednisolone. J Clin Invest 66:243-53, 1980.

76. Bolton WK, Scheld WM, Spyker DA, Overly TL, Sande MA: Pharmacokinetics of moxalactam in subjects with varying degrees of renal dysfunction. Moxalactam in subjects with renal dysfunction. Antimicrob Agents Chemother 18:933-38, 1980.

77. Grogan EL, Sande MA, Clark RE, Nolan SP: Experimental endocarditis in calf after tricuspid valve replacement. Ann Thorac Surg 30, 1980.

78. Hodge RH Jr, Krongaard L, Sande MA, Kaiser DL: Multiple use of disposable insulin syringe-needle units. J Am Med Assoc 244:266-67, 1980.

79. Scheld WM, Brown RS Jr., Harding SA, Sande MA: Detection of circulating antigen in experimental Candida albicans endocarditis by an enzyme-linked immunosorbent assay. J Clin Microbiol 12:679-83, 1980.

80. Sande MA, Scheld WM: Bacterial adherence in endocarditis: interaction of bacterial dextran, platelets, fibrin and antibody. Scand J Infect Dis 24 (Suppl): 100-05, 1980.

81. Sande MA, Scheld WM: Combination antibiotic therapy of bacterial endocarditis. Ann Intern Med 92:390-395, 1980.

82. Giampaolo C, Scheld WM, Boyd J, Savory J, Sande MA, Wills M: Leukocyte and bacterial interrelationships in experimental meningitis. Ann Neurol 9:328-33, 1981.

83. Sande MA, Korzeniowski OM, Allegro GM, Brennan RO, Zak O, Scheld WM: Intermittent or continuous therapy of experimental memingitis due to Streptococcus pneumoniae in rabbits: preliminary observations on the postantibiotic effect in vivo. Rev Infect Dis 3:98-109, 1981.

84. Wenzel RP, Osterman CA, Donowitz LG, Hoyt JW, Sande MA, Martone WJ, Peacock JE, Levine JI, Miller GB Jr.: Identification of procedure-related nosocomial infections in high-risk patients. Rev Infect Dis 3:701-07, 1981.

85. Scheld WM, Spyker DA, Donowitz GR, Golton WK, Sande MA: Moxalactam and cefazolin: comparative pharmacokinetics in normal subjects. Antimicrob Agents Chemother 19:613-19, 1981.

86. Giampaolo C, Scheld WM, Savory J, Sande MA, Wills WR, Boyd JC: A multivariate approach to prognostication in experimental bacterial meningitis. Am J Clin Pathol 76:442-49, 1981.

87. Gwaltney JM Jr., Sydnor A Jr., Sande MA: Etiology and antimicrobial treatment of acute sinusitis. Ann Otol Rhinol Laryngol 90 (Suppl): 68-71, 1981.

88. Bolton WK, Scheld WM, Spyker DA, Sande MA: Pharmacokinetics of cefoperazone in normal volunteers and subjects with renal insufficiency. Antimicrob Agents Chemother 19:821-25, 1981.

89. Scheld WM, Zak O, Vosbeck K, Sande MA: Bacterial adhesion in the pathogenesis of infective endocarditis: effect of subinhibitory antibiotic concentrations of streptococcal adhesion in vitro and the development of endocarditis in rabbits. J Clin Invest 68:1381-84, 1981.

90. Scheld WM, Calderone RA, Alliegro GM, Sande MA: Yeast adherence in the pathogenesis of Candida endocarditis. Proc Exp Biol Med 168:208-13, 1981.

91. Oblinger MJ, Bowers JT, Sande MA, Mandell GL: Moxalactam therapy versus standard antimicrobial therapy for selected serious infections. Rev Infect Dis 4 (Nov-Dec Suppl): S639-49, 1982.

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93. Scheld WM, Giampaolo C. Boyd J, Savory J, Wills MR, Sande MA: Cerebrospinal fluid prognostic indices in experimental pneumococcal meningitis. J Lab Clin Med 100:218-29, 1982.

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95. Scheld WM, Johnson ML, Gerhardt EB, Sande MA: Clindamycin therapy of experimental Staphlococcus aureus endocarditis. Antimicrob Agents Chemother 21:646-49, 1982.

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98. Ernst JD, Sande MA: Antibiotic combinations in experimental infections in animals. Rev Infect Dis 4:302-10, 1982.

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100. Siegel D, Sande MA: Patterns of antibiotic use in a busy metropolitan emergency room: analysis of efficacy and cost-appropriateness. West J Med 138:737-41, 1983.

101. Gualtieri RJ, Donowitz GR, Kaiser DL, Hess CE, Sande MA: Double-blind randomized study of prophylactic trimethoprim-sulfamethoxazole in granulocytopenic patients with hematologic malignancies. Am J Med, 1983.

102. Chambers HF, Korzeniowski OM, Sande MA, and the National Collaborative Endocarditis Study Group: Staphylococcus aureus endocarditis: clinical manifestations in addicts and nonaddicts. Medicine 62:170-177, 1983.

103. Scheld WM, Sande MA: Bactericidal versus bacteriostatic antibiotic therapy of experimental pneumococcal meningitis in rabbits. J Clin Invest 71:411-419, 1983.

104. Simon GL, Smith RH, Sande MA: Emergence of rifampin-resistant strains of Staphylococcus aureus during combination therapy with vancomycin and rifampin: a report of two cases. Rev Infect Dis 5 (Suppl 3): S507-S508, 1983.

105. Hackbarth CJ, Ernst JD, Sande MA: Inhibition of isolation of Escherichia coli in blood cultures by trimethoprim-sulfamethoxazole. J Infect Dis 147-964-965, 1983.

106. Drake TA, Sande MA: Studies of the chemotheapy of endocarditis: correlation of in vitro, animal model, and clinical studies. Rev Infect Dis 5 (Suppl 2): S345-S354, 1983.

107. Ernst JD, Decazes JM, Sande MA: Experimental pneumococcal meningitis: the role of leukocytes in pathogenesis. Infect Immun 41:275-279, 1983.

108. Ernst JD, Rusnak M, Sande MA: Combination antifungal chemotherapy for experimental disseminated candidiasis: lack of correlation between in vitro and in vivo observations with amphotericin B and rifampin. Rev Infect Dis 5 (Suppl 3)S626-S630, 1983.

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110. Scheld WM, Calderone RA, Brodeur JP, Sande MA: Influence of preformed antibody on the pathogenesis of experimental Candida albicans endocarditis. Infect Immun 40:950-055, 1983.

111. Drake TA, Hackbarth CF, Sande MA: Value of serum tests in combined drug therapy of endocarditis. Antimicrob Agents Chemother 24:653-657, 1983.

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DECLARATION OF MERLE SANDE, M.D.

I, Merle Sande, 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 Washington School of Medicine, and received my M.D. from that institution in 1965. From 1965 to 1969, I did my internship and residency at New York Hospital in New York, New York. From 1969 to 1971, I was a Clinical Instructor in Medicine at the University of Texas Medical School in San Antonio and was a Captain in the United States Air Force, based at Lackland Air Force Base. I spent the next eight years teaching courses at the University of Virginia in the field of infectious diseases. I am board certified in the fields of Infectious Diseases and Internal Medicine, and have worked in these fields for fifteen years. I have published approximately 200 professional papers, edited three textbooks, and served on numerous national boards and as a national consultant in infectious diseases. A copy of my curriculum vitae is attached hereto as Exhibit 1 and is incorporated herein by reference as though fully set forth.

2. At present, I am a Professor of Medicine and Vice Chairman of the Department of Medicine at the University of California at San Francisco ("UCSF"). I am also Chief of Medical Services at San Francisco General Hospital ("SFGH"). I have held those positions since 1980.

3. As Chief of Medical Services at SFGH, I am responsible for the care of all patients who come to that facility and have under my direct supervision approximately fifty full-time faculty members, one hundred house staff, and thirty post graduate fellows in various medical specialties. In addition to doing research on numerous bacterial infections, I have also been directly involved in the care of patients with viral and bacterial infections. I have also been involved with epidemics of menigicocccal meningitus, microplasma pnuemonia, and influenza.

4. I have been extensively involved with AIDS, defined herein 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 immunity deficiency such as Kaposi's Sarcoma, central nervous system lymphoma, or infections such as pneumocystis pneumonia). I saw my first case of AIDS in the spring of 1982. Since that time, I have been directly involved in strategies for caring for AIDS patients, developing infectious control measures, and administering research and patient care funds.

The AIDS ward at SFGH is under my direction, along with Drs. Volberding and Wolfsey. I direct the house staff in the care of AIDS patients, and am currently involved in numerous studies on the various expressions of the disease and its diagnostic and therapeutic oddities. I personally have seen and

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participated in the care of approximately 100 AIDS patients at SFGH.

As Chairman of UCSF's AIDS task force, I have been intensively involved in infection control measures dealing with this patient population. Our decisions regarding infectious control were published in September, 1983 in the New England Journal of Medicine and have been adapted worldwide. I am currently aiding in studies at SFGH dealing with the risk of AIDS to health care workers. An additional assignment has been my appointment as Chairman of a UCSF task force whose responsibility is to dispense approximately 3 and a half million dollars of state-directed funds for AIDS research to schools related to the Univerity of California. I have also lectured widely in the United States and Europe on the field of AIDS and next week am running a symposium in Washington, D.C. with the four most prominent experts in the field.

5. AIDS is a disease that is characterized by the elimination and destruction of T-cells, which are responsible for the cellular immune response through which the body responds to malignancies and various pathogens. Destruction of these cells leads to severe immunological impairment, which results in the development of various malignancies and incredibly severe opportunistic infections. An antibody directed against a retrovirus known as HTLVIII, or LAV, has been identified and is present in the majority of patients with AIDS. This virus is labile and easily killed by physical means, such as soap and heat

To my mind, the most amazing aspect of this disease has been the fact that it has remained within certain high-risk groups, namely: homosexual males, intravenous drug abusers, individuals who have received blood or blood products, persons who have had direct contact with equatorial Africa or Haiti, sexual partners of any of the other high-risk groups and, finally, offspring of patients with AIDS. All evidence suggests that it is very difficult to transmit this virus from person to person unless there is direct sexual contact or an exchange of blood products. This view is supported by the fact that, to date, not a single health care worker or person directly involved in the care of AIDS patients and who is not a member of one of the high-risk groups noted above has developed the disease. Early studies also indicate that these health care workers do not have antibody to the virus.

We have evidence that the virus may have sprung out of equatorial Africa and has been there for a period of time. In my opinion, the reason that the disease did not spread rapidly at that time and place is because there was no "multiplier." It now appears clear that promiscuous homosexual sex in the United States has been the key multiplier, in addition to the exchanging of needles in the intravenous drug-abusing population.

6. Data showing that the AIDS disease has spread widely in the gay community have come from a number of different cities. The most impressive data comes from San Francisco, where the CDC and San Francisco Public Health Department co-sponsored

program beginning in 1978 and aimed at determining the natural history and protectiveness of the hepatitis B vaccine. They originally enlisted approximately 6,800 predominantly gay males, from which they recently selected 770 for further study. Blood sera obtained from these individuals in 1978 and retrospectively tested for antibody to the AIDS virus shows that between 1978 and 1980, less than 6 percent were positive for the AIDS virus. By 1984, using a test that does not pick up all the positives, the percentage had increased to 65 percent. The actual percentage is more likely in the 70-80 percent range. Whether the data from this representative patient population can be extrapolated into the rest of San Francisco's gay population is unknown, but the data certainly indicates that a large number of the gay population in fact has come into contact with the AIDS virus.

Testing of control groups of females and heterosexual males has shown that the incidence of positive antibody tests is less than 1 percent. This includes studies performed both at the CDC and on blood donors. Recent studies done at UCSF by Dr. Jay Levy supports the initial observation that antibodies to this retrovirus are essentially absent from the straight population and non high-risk groups. It is also of interest that studies in New York City show that the antibody prevalence to this AIDS agent in intravenous drug abusers approaches 60 to 80 percent.

7. As I have previously indicated, transmission of the virus appears to be quite difficult, if not impossible, by casual contact and to the best of our knowledge is transmitted through

the exchange of infected body secretions. The best bet at the present time is that the virus is found in high concentrations ir semen and that the exchange of semen between individuals represents the most likely and most important mode of transmission. There is also strong data suggesting that the exchange of infected blood from one individual to another is alsc an important mode of transmission. But of equal interest is the fact that, to date, patients who have received accidental needle sticks from patients with AIDS have not developed the antibody and therefore have not been infected by that mode. All this dat suggests that it takes a fairly intensive exposure that may be related to dose of either semen or blood products. The virus ha also been shown to have been transmitted in utero from infected mothers to their offspring. However, other children in the family have not become infected, so it appears that close contac between mother and child is not now associated with transmission

8. In San Francisco, the disease has been found almost exclusively in the gay community. The most common mode of transmission is most likely due to rectal intercourse. We canno say that it is not transmitted through oral intercourse, but believe that the likelihood of the disease being spread by kissing is unlikely. The data strongly suggests that the number of different sexual contacts is a dominant risk factor in the spread of this disease and undoubtedly represents the "multiplier" that was required to initiate the epidemic. However, there is also data suggesting that vaginal intercourse

may also transmit the disease in that there have been female sexual partners of bisexual males who have acquired the disease. Also, in equatorial Africa, female prostitution is apparently one of the leading risk factors. Still unclear is whether the transmission of the virus requires a break in the mucosal barriers of the mouth or the rectum in order to transmit the disease. However, it is likely that the spread would be facilitated by traumatic sexual practices that lead to bleeding, such as "fisting" or other traumatic anal intercourse.

9. The aspect of the AIDS epidemic that has most affected me personally has been the impact of the disease on San Francisco General Hospital. At present, the disease is doubling every eight months, and all evidence suggests that it will continue along these lines indefinitely. About a year ago, our AIDS ward opened at SFGH with twelve beds, which was ample to handle the patient load at the time. Yesterday we had twenty-eight patients in the hospital. At this rate, if measures are not taken to distribute this patient population, a year from now we will have nearly 100 patients in the hospital and would have reached the point where our current services and facilities would be overloaded. Within the next three years, San Francisco will be facing an incredibly severe problem that will become increasingly obvious in terms of caring for this patient population. The City will also incur an enormous financial loss because, at current rates, each patient's care will cost approximately $100,000 from initial diagnosis to death. If, as

we suspect, a high percentage of the gay community is already infected with the AIDS virus and if this equates itself with significant disease, we can expect to have as many as 20,000 or 30,000 patients in the City before the epidemic reaches its peak. The impact on the San Francisco General Hospital is such that we can predict that within several months to a year, we will be unable to fulfill our mission and commitment to the City's non-AIDS population.

10. I have been asked, as an expert in the field, what I would recommend as a strategy for the prevention of AIDS. My response is that since it is unlikely the disease would be spread in a community that was not heavily involved in multiple sexual encounters, the best strategy would be to find some way to stop the sexual practices that transmit the disease. Thus, to the extent education would be effective in reducing this behavior, the expected end result would be a reduction in the spread of the disease. Another approach would be to eliminate places or establishments where these sexual practices are facilitated -- where the ease of having anonymous sex and finding multiple sexual partners is increased. Therefore, it has been my feeling for the past year and a half that a positive move by the San Francisco Department of Public Health Department along these lines would have a significant impact and effect on the spread of AIDS.

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In my judgment, the data currently available allows us to state categorically that the anonymous and multiple sexual encounters encouraged, fostered, facilitated and promoted by bathhouses, sex clubs, and similar facilities in San Francisco has a strong and dramatic effect on the spread of AIDS. I therefore believe it is the obligation of the San Francisco Department of Public Health to make a strong and definite statement regarding the control of this behavior and to close any facilities under its jurisdiction where such activities are being carried out. Physicians and public health officials have a special responsibility to examine the data and make a strong statement regarding this serious epidemic.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct.

Executed on October 6, 1984, at San Francisco, California.

MERLE SANDE, M.D.

3384D

CURRICULUM VITAE
Revised - 9/1/96

NAME: John L. Ziegler, M.D.
DATE & PLACE OF BIRTH: October 28, 1938, New York, New York
MARITAL STATUS: Married

EDUCATION:
1956-60 Amherst College, Amherst, MA, BA (English)
1960-64 Cornell University Medical College, New York, NY, MD

EMPLOYMENT AND APPOINTMENTS:
1964-66 Intern and Assistant Resident, Second (Cornell) Medical Division, Bellevue Hospital, New York, NY (Fellow, Department of Medicine, Cornell University Medical College)

1966-67 Clinical Associate, Medicine Branch, National Cancer Institute, and Admitting Officer, National Cancer Institute

1967-72 Director, Uganda Cancer Institute, Makerere University Medical School, Kampala, Uganda; Senior Investigator, Medicine Branch, National Cancer Institute

1972-75 Chief, Pediatric Oncology Branch, Division of Cancer Treatment, National Cancer Institute

1975-80 Deputy Clinical Director, National Cancer Institute and Associate Director, Clinical Oncology Program, Division of Cancer Treatment, National Cancer Institute

1980-81 Editor-in-Chief, Journal of the National Cancer Institute, National Cancer Institute

1981-96 Associate Chief of Staff for Education and Staff Physician, Veterans Affairs Medical Center, San Francisco, California; Professor of Medicine in Residence, School of Medicine, University of California, San Francisco

1994-96 Senior Scientist (on detail from Department of Veterans Affairs), International Agency for Research on Cancer, World Health Organization, Lyon, France. On special assignment to Makerere University, Kampala, Uganda.

CERTIFICATION:
Diplomate, American Board of Medical Examiners (June 1964)
Qualified, American Board of Internal Medicine (October 1970)
Diplomate in Internal Medicine (October 1973)
Diplomate in the Subspecialty of Oncology, American Board of Internal Medicine (October 1973)
License to practice medicine (New York State, Washington, D.C.)
Certificate, Intensive Course on Epidemiology and Statistics, London School of Hygiene and Tropical Medicine (June 1993)
Candidate, M.Sc. Epidemiology, London School of Hygiene and Tropical Medicine (Sept. 1997)

PROFESSIONAL SOCIETIES:
American Association for Cancer Research 1968-81
American Federation of Clinical Research 1972-92
American Society of Clinical Investigation 1973-
American Society of Clinical Oncology 1968-
American Society of Hematology 1968-81
Association of Physicians of East Africa 1967-72
Association of Surgeons of East Africa (Honorary) 1967-72

Uganda Medical Association 1967-72
Council of Biology Editors 1980-81
Western Association of Physicians 1983-
Western Society for Clinical Investigation 1983-

MEMBERSHIP (selected activities):

American Cancer Society's Scientific Advisory Committee for Clinical Investigations (Immunology and Immunotherapy) 1974-77; (Chemotherapy) 1982-85, Chairman
Immunotherapy Committee, Tumor Immunology, National Cancer Institute 1973-75
Medical Board, Clinical Center, National Institutes of Health 1975-80
Clinical Research Committee, National Cancer Institute (Chairman) 1975-80
American Joint Committee for Cancer Staging and End Results Reporting 1976-80
Consultant, SEER Program, Division of Cancer Cause and Prevention, NCI 1977-79
Editorial Board, Cancer Chemotherapy Reports, 1975-78
Consultant, National Bladder Cancer Task Force 1978-80
Scientific Advisor, NCI Bladder Cancer Project, Cairo, Egypt 1973-79
Consultant, Institute of Medicine, National Academy of Sciences (Workshop on Research in Developing Countries) 1979
Admissions Committee, Uniformed Services University for the Health Sciences, Appointment by Surgeon General, USPHS 1980-81
Executive Committee, Northern California Oncology Group 1982-84
Corresponding Editor, West African Journal of Medicine 1986-
Member, Chief Medical Director's Steering Committee on AIDS, Veterans Administration Central Office 1987-89
Consultant, World Health Organization 1986, 1987, 1988
Trustee (appointed by the President, University of California), Marin Community Foundation 1988-90
Member, National Task Force for the NIH Strategic Plan (Population-based Studies) July, 1992
Chairman, Steering Committee, Pilot Evaluation of AIDS Retrovir Treatment in Africa (WHO, Family Health International, Burroughs Wellcome Co.) 1992-93

ACADEMIC APPOINTMENTS:

1967-72	Honorary Lecturer in Medicine, Makerere University Medical School, and Honorary Senior Registrar, Mulago Hospital, Kampala, Uganda; Lecturer in Surgery, Harvard College; Clinical Associate Professor, Cornell University Medical College
1976-78	Associate Clinical Professor of Medicine, George Washington University Medical School
1979-81	Associate Clinical Professor of Medicine, Georgetown University School of Medicine
1980-81	Professor of Medicine, Uniformed Services University of the Health Sciences
1990-91	Visiting Fulbright Professor of Medicine, Makerere University Medical School, Kampala, Uganda (on Sabbatical leave from UCSF)
1992-93	Visiting Professor, University of Cambridge and Associate, Darwin College
1992-96	Visiting Professor, London School of Hygiene and Tropical Medicine
1994-96	Visiting Fulbright Professor of Medicine, Makerere University Medical School, Kampala, Uganda
1995-96	Visitor Oxford University

MILITARY SERVICE:

1966-81	Medical Director, U.S. Public Health Service

AWARDS:

United States Public Health Service Commendation Medal, July 1969
Albert and Mary Lasker Award, November 1972
Heath Award, M.D. Anderson Hospital, November 1983
Fulbright Research Scholar, Makerere University, Kampala, Uganda, 1990-91
Howard Gilman Foundation Honors Program Lecturer, New York University, 1991
Fulbright Research Scholar, Makerere University, Kampala, Uganda, 1994-95

RESEARCH ACTIVITY AT UCSF AND VA:

1981-82	Principal Investigator for a $50,000 grant awarded from American Cancer Society to establish Kaposi's sarcoma clinic at UCSF (with Drs. Conant and Volberding)
1983-86	Co-Principal Investigator (with Dr. P. Volberding): Cooperative Agreement on Laboratory and Clinical Studies of AIDS (NCI, $1.4 million)
1983-85	Co-Principal Investigator (with Dr. H. Lichtenstein): National Institute of Aging Academic Award ($78,000, terminal year) to establish geriatric teaching program at VA Medical Center
1985-92	Director, AIDS Clinical Research Center, University of California San Francisco (State funded, $1.1 million annually)
1986-89	Co-Principal Investigator (with Prof. L. Zegans): AIDS Professional Education Program (NIMH contract, $400,000)
1987-92	Co-Principal Investigator (with Dr. Volberding): Program Project Grant on Laboratory and Clinical Studies in AIDS (NIAID, $3.66 million for 5 years)
1987-92	Associate Investigator (Dr. Susan Allen, PI): African AIDS: Risk Factors, Virology and Pathology (NIAID, $1.5 million for 5 years)
1987-92	Co-Principal Investigator (with Dr. P. Jensen): VA Cooperative Study (298) on Zidovudine in Patients with ARC (Veterans Administration $510,993 for 3 years)
1988-93	Associate Investigator (Dr. Elizabeth Holly, PI): Epidemiology of Non-Hodgkin's Lymphoma and Retroviruses (NCI, $4.3 million for 5 years)
1988-94	Associate Investigator, Center for AIDS Prevention Studies, (Dr. Stephen Hulley, PI): International Training Program in AIDS Epidemiology (NIMH/NIDA, $10 million for 5 years)
1988-93	Director, VA Center for AIDS Research and Education and Director, AIDS Clinical Unit (Veterans Administration, $1.5 million for 5 years)
1988-90	Chairman, 6th International Conference on AIDS, San Francisco, June 20-24,
1988-93	Co-Principal Investigator with Dr. P. Volberding, UCSF Center for AIDS Research (NIAID, $4.1 million for 5 years)
1988-93	Associate Investigator: Case-Control Partner Study on HIV Transmission in Uganda (Rockefeller Foundation, $330,000)
1989-90	Chairman, Scientific Advisory Committee, Substance Abuse Treatment Research Unit (NIDA, $8.7 million for 5 years)

1990-91 Visiting Fulbright Professor, Makerere University Medical School, Ministry of Health, Kampala, Uganda

1992-93 Consultant, Family Health International. AIDS Treatment Initiative in Developing Countries.

1994-95 Visiting Fulbright Professor, Makerere University Medical School, Ministry of Health, Kampala, Uganda

1994-96 Senior Scientist, International Agency for Research on Cancer, WHO. Principal Investigator, "Case-Control Study of Kaposi's Sarcoma in Uganda." CDC-VAMC Interagency Research Agreement ($530,000).

TEACHING:

Oncology Attending, VA Medical Center, 3 months/year
Oncology Attending, Moffitt Hospital, 1 month/year
Medicine Attending, VAMC, 1 month/year
Introduction to Clinical Medicine Preceptor, VAMC, 2 months/year
Problem Solving Course for First Year Students, 2 months/year
Director, Postgraduate Program in Medicine (M. Med. Degree), Dept. of Medicine, Makerere University Medical School, Kampala, Uganda, 1990-91
Visiting Professor, London School of Hygiene and Tropical Medicine (Taught in DTM&H Course, and advised M.Sc. students) 1992-94
Visiting Professor, University of Cambridge, School of medicine, Addenbrooks Hospital, Cambridge, U.K. (Taught introduction to Clinical Medicine) 1992-93
Faculty Advisor, M.Med Program, Makerere University Medical School, Kampala, Uganda, 1994-96

COMMITTEES:

UCSF University Governance (summary, 1981-91): Committee on Education, (Academic Senate), Curriculum Committee, Subcommittee on Evaluation, Residency Review Committee, Research Evaluation and Allocation Committee, Advisory Committee on Postdoctoral Affairs, Education Policy Committee, Universitywide Committee in Geriatrics, Editorial Board of UCSF Magazine, Dean's AIDS Advisory Committee (ex officio), Chancellor's Advisory Council on AIDS, member, UCSF Comprehensive Cancer Center, member, Cancer Research Institute

Veterans Administration Medical Center: Clinical Education Committee (Chair), Learning Resources Advisory Committee (Chair), Medical Executive Board, AIDS Coordinating Committee, Dean's Committee, Clinical Advisory Committee

BIBLIOGRAPHY:

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1. Ziegler, JL and Miller, DG: Lymphosarcoma resembling the Burkitt tumor in a Connecticut girl. JAMA 198:1071-1073, 1966.

2. Ziegler, JL, Cohen, MH, Vogel, CL, Sheagren, JN and Carbone, PP: Immunologic studies in American patients with Burkitt-like lymphoma. Cancer Res 26:2527-2531, 1967.

3. Ziegler, JL, Carbone, PP, Berard, CW and Thomas, LB: Burkitt's tumor in the United States: Diagnosis, treatment and prognosis. In Clifford, Linsell and Timms (eds.): Cancer in Africa, East Africa Publishing House, Nairobi, 1968, pp. 239-251.

4. Carbone, PP, Berard, CW, Bennett, JM, Ziegler, JL, Cohen, MH and Gerber, P: Burkitt's tumor: Combined clinical staff conference at the National Institutes of Health. Ann Int Med 70:817-832, 1969.

5. Cohen, JMH, Bennet, JM, Berard, CW, Ziegler, JL, Vogel, CL, Sheagren, JN and Carbone, PP: Burkitt's tumor in the United States. Cancer 23:1259-1272, 1969.

6. Cohen, MH, Ziegler, JL and Carbone, PP: Burkitt's tumor in the United States. The Cancer Bulletin 20:68-74, 1969

7. Henle, G, Henle, W, Clifford, P, Diehl, V, Kafuko, GW, Kirya, BG, Klien, G, Morrow, RH, Manube, GMR, Pike, P, Tukei, P and Ziegler, JL: Antibodies to EB virus in Burkitt's lymphoma and control groups. J Nat Cancer Inst 43:1147-1157, 1969.

8. Brown, CH, Ziegler, JL, Templeton, C and Carbone, PP: Cyclophosphamide toxicity in Ugandan and American patients with lymphoma. Cancer 26:462-467, 1970.

9. Fass, L, Ziegler, JL, Herberman, RB, and Morrow, RH: Evaluation of the effect of remission plasma on untreated patients with Burkitt's lymphoma. J Nat Cancer Inst 44:145-149, 1970.

10. Fass, L, Herberman, RB, Ziegler, JL: Delayed cutaneous hypersensitivity to autologous extracts of Burkitt's lymphoma cells. New Eng J Med 282:776-780, 1970.

11. Ziegler, JL, Cohen, MH, Morrow, RH, Kyalwazi, SK and Carbone,.PP: Immunologic studies in Burkitt's lymphoma. Cancer 25:734-739, 1970.

12. Ziegler, JL, Morrow, RH, Bluming, AZ, Fass, L, Templeton, AC, Templeton, C and Kyalwazi, SK: Clinical features and treatment of childhood lymphoma in Uganda. Int J Cancer 5:415-425, 1970.

13. Ziegler, JL, Morrow, RH, Fass, L, Kyalwazi, SK, Carbone, PP: Treatment of Burkitt's lymphoma with cyclophosphamide. Cancer 26:474-484, 1970.

14. Ziegler, JL, Bluming, AZ, Morrow, RH, Fass, L and Carbone, PP: Central nervous system involvement in Burkitt's lymphoma. Blood 36:718-728, 1970.

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21. Henle, G, Henle, W, Clifford, P, Diehl, V, Kafuko, GW, Kirya, BG, Klein, G, Morrow, RH, Manube, GMR, Pike, P, Tukei, PM and Ziegler, JL: Antibodies to Epstein-Barr virus in Burkitt's lymphoma and control groups. J Nat Cancer Inst 43:1147-57, 1969.

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26. Bluming, AZ, Ziegler, JL and Carbone, PP: Bone marrow involvement in Burkitt's lymphoma: Results of a prospective study. Brit J Hemat 22:369-376, 1972.

27. Ziegler, JL, Bluming, AZ, Magrath, IT and Carbone, PP: Intensive chemotherapy in patients with generalized Burkitt's lymphoma. Int J Cancer 10:254-263, 1972.

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55. Ziegler, JL and Kyalwazi, SK: Recent research in Burkitt's lymphoma. East Afr Med 49:670-675, 1971.

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61. Ziegler, JL: Burkitt's lymphoma: Lessons for the oncologist, In Recent Advances in Management of Children with Cancer, Tokyo, pp. 158-163, 1980.

62. Ziegler, JL: Medical progress. Burkitt's lymphoma. N Eng J Med 305:735-745, 1981.

BURKITT'S LYMPHOMA/Chapters in Books

63. Ziegler, JL: Burkitt's lymphoma. In Shaper, Kibukamusoke and Hutt (eds.): Medicine in a Tropical Environment, St. Alban's, Knight & Co., Ltd., 1971, pp. 360-371.

64. Ziegler, JL and Burchenal, JH: Treatment of Burkitt's tumor. In Molander and Pack (eds.): Lymphosarcoma and Related Diseases, Charles C. Thomas, New York, 1974, Chap. 12, pp. 332-342.

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68. Ziegler, JL and Magrath, I: Treatment of Burkitt's lymphoma. In Deeley (ed.): Malignant Diseases in Children, Buttersworth, London, 1974, pp. 360-371.

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77. Ziegler, JL: Burkitt's lymphoma: lessons for the oncologist. In Ford, RJ, Fuller, CM, Hagemieister, FB (eds.): New Perspectives in Human Lymphoma, 1984, pp. 439-452.

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78. Master, SP, Taylor, JL, Kyalwazi, SK and Ziegler, JL: Immunologic studies in Kaposi's sarcoma in Uganda. Brit Med J 1:600-602, 1970.

79. Taylor, JL, Templeton, AC, Vogel, CL, Ziegler, JL and Kyalwazi, SK: Kaposi's sarcoma in Uganda: A clinicopathological study. Int J Cancer 8:122-135, 1971.

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81. Olweny, CLM, Kaddamukasa, A, Atine, I, Owor, R, Magrath, IT and Ziegler, JL: Childhood Kaposi's sarcoma: Clinical features and therapy. Brit J Cancer 33:555, 1976.

82. Drew, WL, Conant, MA, Miner, RC, Huang, ES, Ziegler, JL, Groundwater, JR, Gullet, JH, Volberding, PA, Abrams, DI and Mintz, L: Cytomegalovirus and Kaposi's sarcoma in young homosexual men. Lancet 2:125-127, 1982.

83. Levy, JA and Ziegler, JL: Hypothesis. Acquired immunodeficiency syndrome is an opportunistic infection and Kaposi's sarcoma results from secondary immune stimulation. Lancet 2:78-81, 1983.

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85. Ammann, AJ, Schiffman, G, Abrams, D, Volberding, P, Ziegler, J, Conant, M: Acquired B-cell immunodeficiency in acquired immunodeficiency disease. JAMA 251:1447-1449, 1984.

86. Ziegler, JL, Beckstead, JH, Volberding, P, et al.: Non-Hodgkin's lymphoma in 90 homosexual men. Relationship to generalized lymphadenopathy and acquired immunodeficiency syndrome. N Eng J Med 311:565-570, 1984.

87. Ziegler, JL, Bragg, L, Abrams, DI, et al.: High grade Non-Hodgkin's lymphoma in patients with AIDS. Ann NY Acad Sci 437:412-419, 1984.

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91. Volberding, PA, Abrams, DI, Conant, M, Kaslow, K, Vranizen, K and Ziegler, JL: Vinblastine therapy of Kaposi's sarcoma in AIDS. Ann Int Med 103:335-338, 1985.

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93. Kahn, JO, Kaplan, LD, Ziegler, JL, Volberding, PA, Crowe, S, Saks, S, Abrams, DI: Intralesional recombinant tumor necrosis factor-alpha for AIDS associated Kaposi's sarcoma. J AIDS 2:217-223, 1989.

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96. Ziegler, JL. Endemic Kaposi's sarcoma and local volcanic soils. Lancet 342:1348-51, 1994.

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98. Ziegler, JL: Kaposi's sarcoma in homosexual men. JNCI 68:337-338, 1982.

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Note to Index: When an organization or entity is known primarily by its acronym and referred to primarily by its acronym in the text, it is indexed under the acronym. Otherwise full titles are given, followed by the acronym. Examples: HIV [human immunodeficiency virus], NIH [National Institutes of Health]; but General Accounting Office [GAO]

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