

Abstract

Dr. Bruce Chabner of the National Cancer Institute (NCI), focuses on NCI's first AIDS related conference and the people involved. He also describes the flexibility of NIH's intramural program, the shift from NCI to NIAID as the focal point of AIDS research, and early congressional hearings and legislative actions. The difference in the NIH's and the CDC's approach to new diseases, early efforts by NCI's director, Dr. Vincent DeVita, issues of early safety hazards, and funding after the conference are briefly reviewed. He also touches upon his research before the detection of AIDS.

This is an interview with Dr. Bruce Chabner, National Cancer Institute (NCI), National Institutes of Health (NIH) at Bethesda, Maryland. The interview was conducted on 17 November 1989 by Dennis Rodrigues, program analyst, NIH Historical Office.

Rodrigues: Would you begin by discussing your background, training, research experience, and how you became involved with the Kaposi's sarcoma and Pneumocystis carinii pneumonia (PCP) outbreaks?

Chabner: I am a medical oncologist. I came to NIH as an officer in the Public Health Service in 1967 during the Vietnam War. I spent two years in the intramural program in a training position. I left and came back in 1971 as a permanent employee and have been here ever since. My major interests have been in cancer drugs and in medical oncology. In 1981, I became the head of the Division of Cancer Treatment, which has the major responsibility for drug development and

also has an interest in lymphoma and related diseases. It was in that capacity that I first became aware of the Acquired Immunodeficiency Syndrome [AIDS].

As I remember, I came into this job in July 1981, and it was that summer that we first noticed some unusual cases of immunodeficiency. I am not sure, but I think in one instance it was associated with either Kaposi's [sarcoma] or a lymphoma. The patient had Mycobacterium avium intercellulari, and a very profuse amount of involvement of the marrow with this infection. Sam [Dr. Samuel] Broder pointed this case out to me. We began to hear about other patients who had immune deficiency and also about an increase in Pneumocystis. At the same time, in our division, Bob [Dr. Robert] Gallo had just discovered the T-cell lymphotropic viruses, HTLV-1 [Human T-cell leukemia virus-type 1]. We made the connection that there might be a relationship here between the viral illness and the immunodeficiency syndrome that was being reported. There were a few cases; the CDC [Centers for Disease Control] was reporting increases of Pneumocystis pneumonia. In September 1981 we organized the first meeting about AIDS that was held in this country. Its purpose was to discuss the clinical syndrome and the possible etiologies. I talked to Bob Gallo, and he expressed some interest in it, although he was busy doing some other things. He really did not get involved with AIDS research until about a year later, as I remember.

Rodrigues: Getting back to the September 1981 conference, who were some of the other individuals involved in planning it?

Chabner: I can provide you with the documents. They are in my files. I was the acting director of the division. I subsequently became the permanent director. [Dr.] Saul Schepartz was the deputy. He really did not have a role in initiating this. Sam Broder was the head of the Clinical Oncology Program, and Sam did have a significant role in this because he was the one who first noticed this target case in the clinical serials [journals]. He brought it to my attention. [Dr.] Arthur Levine may have been involved, but I just do not remember when Arthur came over.

Rodrigues: One of the names I came across was a Dr. William DeWys?

Chabner: DeWys? Bill DeWys. Yes. I believe that Bill was working in the Cancer Therapy Evaluation Program in our division and had a role in organizing that first meeting. It is my recollection that I was the first among the administrative staff at NCI who became concerned about the syndrome. But it was because Sam had called my attention to a case. Then, in the fall of 1981 or in early 1982, I got Arthur Levine interested in it, and Arthur made some suggestions about attempting to isolate viruses about six months to a year later. But the etiology of this was actually discussed at the 1981 conference. You can get the program and see. I remember clearly that one of the reasons that we were interested in the disease was the possible connection with the HTLV viruses.

Rodrigues: How about Dr. John Ziegler? Does that name ring a bell?

Chabner: John was interested in this. But I do not know what he was doing in those days. He had been in Africa and he had done some work on Kaposi's sarcoma. I do not

think John had a significant role in the conference. I think he had been bounced out of his position at that point. He had been director of the Clinical Oncology Program. He was doing something else. I cannot remember what he was doing. He had been relieved of that job. He had been interested for some time in Kaposi's and in Burkitt's [lymphoma], and I guess he became interested in AIDS later. When he went out to San Francisco, he got into AIDS. He was one of the first people to describe these second tumors in AIDS--lymphomas. When he was here [at the NIH], he never had any significant role in this.

Rodrigues: As far as I can tell from looking at various memos and other documents that I have been able to uncover, you seem to be the person who was given the principal responsibility for coordinating activities relating to AIDS at the NIH. I know that you also represented NCI at the April 1982 hearing that Congressman Henry Waxman held in Los Angeles. How would you characterize that hearing? It seems as if there was a great deal of criticism that more should be done about AIDS. But, yet, at the same time, I have also heard that people were not really convinced yet about what was the cause of AIDS.

Chabner: That is right. It also was not a disease that fell naturally within the mandate of the Cancer Institute. Anything we did on it up to that point and even afterwards, was really a function of our own personal interest in the disease. We already had a hunch that we knew what was going on, and it helped. There was no congressional mandate for the Cancer Institute to study AIDS because, in fact, it

was an infectious disease by most people's estimation. If it was not that, it was a toxic disease. It was not a malignancy. So, I could hardly respond to the criticism that the federal government was not doing enough. We were doing more than anyone would have expected us to do.

Rodrigues: There was very little appreciation of the different areas of responsibilities of the different institutes and agencies.

Chabner: Yes. Until it became clear what the cause of this disease was, it was not clear which institute was responsible for it. I think because it was an immunodeficiency disease, the Allergy and Infectious Diseases Institute [National Institute of Allergy and Infectious Diseases, NIAID] probably had the primary role and interest. This certainly became the case after AIDS was demonstrated to be the result of an infection. But up to that point, a lot of different people were working on it; there were people in the Mental Health Institute [National Institute of Mental Health, NIMH] who were interested in it. There still are. [Dr.] Candace Pert was interested in AIDS, and so was the intramural director of NIAID at that time, Dr. Kenneth Sell, who subsequently went to Emory. Dr. Sell had a theory in 1982 that AIDS was caused by a toxin of some sort, a mycotoxin. He and other researchers had done some experiments and saw some peak in the blood, which was total hogwash. But they went off on a tangent about the idea that AIDS was caused by a fungal toxin in the blood. Nobody else really bought that. But there were a lot of theories about what caused AIDS, and because of

that, all sorts of people were working on it. They thought it might be relevant to their interests.

Rodrigues: As a result of the conference held in September 1981, did you to begin to add some supplemental funds to existing grants?

Chabner: Yes, we issued an RFA [Request for Application] for AIDS grants with the Division of Cancer Etiology, and about \$1.25 million in grants was awarded.

Rodrigues: One memo I came across--I cannot recall if it was from Dr. Gallo or Dr. Broder--expressed concern about the samples from AIDS patients that were coming in, because it was not known how dangerous these samples were.

Chabner: Sam was actually hand-carrying samples across to Gallo for a couple of years. He personally transferred samples--lymph node biopsies and serum and other materials--to Gallo's lab. He was firmly convinced that the cause of AIDS would prove to be a virus, and I was, too. That is one of the reasons I got interested in it. In the early 1980s, Bob Gallo was working in our division--he worked with us until 1987, when his laboratory was transferred to the Division of Cancer Etiology. His position in our division was fortuitous, because it gave him good access to clinical specimens.

Rodrigues: How much flexibility as a scientific manager do you have to redirect resources towards some problem that falls within the general area of your responsibility and that you feel is important?

Chabner: A fair amount. The problem is that half of our money is locked up in grants, so

we cannot take grant money away from one person and give it to another. You can emphasize an area through certain new grants that will be made, but that is a small fraction of the pool. Some of our programs are long term, so we cannot just stop them, like drug screening and the drug discovery program for cancer. We would not stop those. But then there is flexibility in the intramural program. Intramural investigators can stop working on one thing and take up something else or shift their work partially toward something else. We can begin with new patients. In fact, the drug development part of it might be the thing we do best here [at NCI]. When it became clear we had some leads about new drugs, we just brought in new patients rapidly. We were limited by beds and nurses, actually. There were some big fights over this with Building 1, some real hot memos. There were some big arguments between us and Dr. [James] Wyngaarden about beds for AIDS patients.

Rodrigues: We have learned that research managers viewed the AIDS problem differently in the context of other priorities and how resources were shifted.

Chabner: People were afraid of AIDS. I remember having an argument in 1981 with the director of our institute, Dr. Vincent DeVita, about what we were going to call AIDS. He was very upset about the fact that we called it an epidemic. He said, "I don't want to hear that term used around here, because that gets people too upset and agitated and worried. We will have public panic if you start calling it an epidemic." He was unconvinced that it was an epidemic. I think that he was

worried that if it were indeed an epidemic, the Cancer Institute's budget would suffer. That is a cynical outlook, but I cannot imagine why else he said it.

Rodrigues: I have heard about his sensitivity to the word "epidemic." Someone suggested that it may have been related to an earlier incident. What appeared to be an epidemic or an outbreak of certain types of lymphomas occurred in some region of the country. It later turned out to be a statistical fluke.

Chabner: Yes. This happened on occasion. There would be clusters of cases. People would call them epidemics of lymphomas or leukemias. But I do not think that was what it was. AIDS was different. There was never very convincing evidence for an epidemic of lymphomas. But, the evidence for the epidemic nature of AIDS was very convincing.

Rodrigues: How would you characterize the presentations that were made at the September 1981 workshop? Was there a lot of excitement?

Chabner: There was. There was tremendous interest in AIDS; tremendous anxiety and concern about what was causing it. The workshop was very well attended, and everybody wanted to get in his or her two cents about what was causing the disease. We all had theories about what the cause was.

Rodrigues: In some of the things that have been written about AIDS, particularly in Randy Shilts's book, the NIH is characterized as a sleepy, ivory-tower citadel of academia. Do you agree?

Chabner: No, that is not true. The people at this meeting were very interested. They were

not only people from the NIH; they were people from all over the place. It was a national meeting. I think it is fair to say that some of the people in higher places were rather "laid-back" about the whole thing. The media have referred to that. I do not know what the congressional testimony looks like. It would be interesting if I could see it. At least people were saying that we had a problem on our hands, even though they might have been saying, "You know, I'm not convinced this is really very important." By 1983 everybody was convinced--surely, even by 1982. In 1981, it took a while before people became convinced that there was a problem.

Rodrigues: For a number of years at the beginning of the AIDS epidemic, the Cancer Institute was the focal point for what was happening at the NIH in relation to AIDS. Do you recall when the shift to NIAID began?

Chabner: It shifted when money started being given to NIAID. When the NIH started getting large budget increases for AIDS, Tony [Dr. Anthony] Fauci became the head of NIAID and was recognized as the leader of the research effort on this campus. He made the determination about where the funds went. He got the balance of the funds. NIAID took responsibility for the extramural programs, which was appropriate. They recruited staff--large numbers of people from our institute went to NIAID. There were some things that did not get shifted over: the drug development program was still at NCI; we still had the intramural drug development effort, patient effort, clinical effort. We also had Gallo's laboratory

and epidemiology. NIAID assumed responsibility for administering programs throughout the country: cooperative trials, AIDS grants--they were very involved with grants. All that took place in the period after 1983, probably in 1984.

Rodrigues: In the legislative arena, Waxman proposed an emergency fund for responding to a future surprise outbreak like AIDS. There seemed to be some debate about whether or not that was a good idea. Some people suggested that it did have some merit but others said that, in the world of biology, it was too difficult to predict when something like AIDS might come along again. It might be next year; it might be in ten years; it might be in a hundred years. Do you tie up a significant amount of money simply for that contingency?

Chabner: We have the CDC to investigate things like this. They have a budget in the millions. A disease problem of this magnitude does not come along every five years or ten years. It happens once in a lifetime. I do not think that a provision for an emergency fund is necessary.

Rodrigues: Traditionally, the NIH has not been involved with incidences where there is an outbreak of a new disease. The NIH does not jump in the same fashion that the CDC does.

Chabner: In this instance, the CDC was the first to publish anything, in Morbidity and Mortality Weekly Report (MMWR). But the CDC did not have the expertise to isolate the virus or work on treatment. That is why we got into it. We were ready to do that kind of research, and they were not. They were there to do the

epidemiology and to point out the fact that an epidemic existed, but, to do research on it in this case, you had to be familiar with the viruses and virology.

Rodrigues: I believe that some NCI epidemiologists were involved. Was it Dr. Joseph Fraumeni's branch that was active?

Chabner: We did a fair amount of epidemiology. Bill [Dr. William] Blattner and--I cannot remember who else. A couple of other people. Bill Blattner and Sam Broder were close friends. Bill Blattner had been working on HTLV-1, and when this came along, he very naturally got deeply involved in it. Bill can tell you a lot about the early days. You also ought to look at the documents. People have funny recollections of things. Inaccurate recollections. None of us has perfect memories about it. I think my memory for the dates is pretty accurate. I think my first inkling that there was something wrong was when I heard about this patient who Sam Broder brought up. He was an Israeli patient who was admitted to Tom [Dr. Thomas] Waldmann's service. I am not certain about this, but I think it was Tom Waldmann's service. He had an unusual infection. Sam asked me to come over and take a look at the marrow.

Rodrigues: Thank you, Dr. Chabner.

Index

AIDS

causes of 6-7, 13
conference on at NIH 2-3, 10-11
Congressional hearing on 5
patients 1-2, 14
Blattner, William 13

Broder, Samuel 2, 3, 7, 13, 14
Burkitt's lymphoma 4
Centers for Disease Control (CDC) 2, 12, 13
Chabner, Bruce
 career 1
 coordinator of AIDS activities at NIH 5
DeVita, Vincent 9
DeWys, William 3
Fauci, Anthony 11
Fraumeni, Joseph 13
Gallo, Robert 2, 7-8, 12
Human T-cell leukemia virus (HTLV) 2, 13
Kaposi's sarcoma 1, 2, 3, 4
Levine, Arthur 3-4
Morbidity and Mortality Weekly Report (MMWR) 13
Mycobacterium avium intercellulari 2
National Cancer Institute (NCI) 3, 5, 9, 11, 12
 as a focal point for AIDS research 11-12
National Institute of Allergy and Infectious Diseases (NIAID) 6
 as a focal point for AIDS research 10, 11-12
National Institute of Mental Health (NIMH) 6
National Institutes of Health (NIH) 1
 and intramural program 8
 first AIDS related conference at 2, 10-11
 grants 8
Pert, Candace 6
Pneumocystis carinii pneumonia (PCP) 1, 2
Request for Application (RFA) 7
Schepartz, Saul 3
Sell, Kenneth 6-7
Shilts, Randy 10
Waldmann, Thomas 14
Waxman, Henry 5, 12
Wyngaarden, James 9
Ziegler, John 4