

***This is an oral history interview with Dr. Amoz Chernoff at his home in Potomac, Maryland, on 28 January 1993 on the NIH response to AIDS. The interviewers are Dr. Victoria A. Harden, Director, NIH Historical Office, and Dennis Rodrigues, Program Analyst, NIH Historical Office.***

Harden: We usually start our interviews by asking if you would give us a summary of your background, that is, your education, your medical training, the reasons why you wanted to go into medicine, and your career up till 1980.

Chernoff: That is a tall order. Suffice it to say that I graduated from medical school back in 1947 and did a medical internship and residency at the Massachusetts General Hospital in Boston and at Barnes Hospital in St. Louis, before deciding to go into hematology as a specialty. I had several years of fellowship training in hematology followed by a faculty appointment at the Washington University School of Medicine. Subsequently, in the mid-1950s, I went to Duke University where I became an associate professor of medicine and chief of the hematology division at the Durham, North Carolina, Veterans' hospital.

I had always been interested in hematology. During my medical school years, I began to develop an interest in the morphology of blood, in part, because of the influence of one of my professors in anatomy, a man named [Dr. Thomas] Tom Dougherty. He got me involved in bone marrow studies and bone marrow related activities, and from that my interest in hematology developed. After a few years at Duke University, a new research operation was opening up under the aegis of the University of Tennessee in Knoxville, Tennessee, and I went there as a research professor. It was about that time that I was awarded a lifetime Research Career Award by the NIH. A few years later I became Director of the Research Center at the University of Tennessee in Knoxville. The center focused on hematologic problems, and encompassed the broad scope of hematology.

Harden: Can I ask you to expand further on your research with hemoglobin and thalassemia?

Chernoff: Starting in my fellowship years at the Michael Reese Hospital in Chicago, I became interested in hereditary hemolytic anemias and the role that abnormal hemoglobins played in their evolution. In fact, I was one of the people who developed a simple test for fetal hemoglobin, the one-minute alkali denaturation procedure, a test which for many years, and perhaps even today, is still used as one of the earliest screening tests for this particular pigment. In any event, I became interested not only in the broad group of sickle cell diseases but also in other hereditary hemolytic anemias which were subsequently found to be related to the abnormal hemoglobin question. In that group of abnormalities are the thalassemias, to which you referred, and that, among other things, led us to study thalassemia in South East Asia and to the discovery of a new hemoglobin called

hemoglobin E, found primarily among Thais. My colleagues and I went to Thailand in the summer of 1954 to study the disease. We began a rather extended effort among the Thais to study the impact of thalassemia in South East Asia. Some thirty years later in 1984, or 1985, our work was honored by a special award from the King of Thailand, and we were invited back to participate in celebratory activities.

Over the years I focused my research primarily on hereditary hemolytic anemias, specifically hemoglobinopathy, but I also had an interest in other aspects of hematology. I did not, in fact, have a significant interest in transfusion related activities until I came to the NIH. There, my focus, while it was in much of the field of hematology, as Director of the Division of Blood Diseases and Resources [DBDR] I did shift to areas more related to transfusion medicine. But to return to the historical aspects in which you are interested, when I reached the University of Tennessee, in 1958 I believe it was, I worked primarily in my own laboratory at the Research Center. As I have indicated, I became Director of the University of Tennessee Memorial Research Center, either in 1964 or 1965, in which capacity I remained for some 13 years. Since I have the philosophy that no leader of an organization ought to stay in the same job for more than ten years, I finally prevailed upon my superiors at the university to find a replacement for me. I then assumed the position of Vice Chancellor for Academic Affairs at the Medical Units of the University of Tennessee in Knoxville, Tennessee.

It was at that time that [Dr. Robert] Bob Levy approached me about becoming Director of the Division of Blood Diseases and Resources at the NIH. With some uncertainty, I made the move to Washington, D.C. I believe it was in 1978. I took over the direction of the division from [Dr.] Wolf Zuelzer, who was my predecessor, and I began to focus on the specific aspects of the program that had been developed under his leadership. My hope in coming to Washington after a very satisfactory career at the University of Tennessee was to try to have some impact primarily on medical education as it relates to hematology. I was very interested in trying to provide a more solid basis for hematologic research in laboratories around the country and among students who were going through the learning process at the various universities. I was a little disappointed in realizing how massive the bureaucracy at the NIH was and also how much inertia the system had, so that no matter what one did it took a long time to discern minimal changes in direction.

Harden: Now, are you talking about the NIH, or more generally?

Chernoff: The NIH generally, and the Division of Blood Diseases and Resources more specifically. I was also troubled by what I thought was an unnatural and unworkable division of the field of hematology among two major institutes, actually among four different institutes, of the NIH. It made it hard to coordinate

many of the things that could have been done with a more cohesive group of people working together. One of my other objectives was to have some impact on unifying hematology at the NIH and perhaps end up with an institute, such as a National Institute of Blood Diseases or a National Institute of Hematology.

Harden: This, of course, is a recurring problem at the NIH. The overlap between the National Institutes of Neurology and Mental Health is another example that comes to mind. But I am trying to recall which four institutes were involved in hematology.

Chernoff: At that time, Arthritis and Metabolic Diseases [National Institute of Arthritis and Metabolic Diseases] had a big chunk of hematology, much smaller than NHLBI [National Heart, Lung, and Blood Institute], but still covering a significant area with some overlap of what we were doing in our Institute. Allergy and Infectious Diseases [National Institute of Allergy and Infectious Diseases] had a large part of the immunology that was often considered part of hematology and then, of course, the Cancer Institute [National Cancer Institute] had all the leukemias, which again are classically a part of hematology. Among those four institutes, while NHLBI probably covered 60 percent of the ground; Arthritis and Metabolic Diseases, or whatever it is called today, covered perhaps 15 to 16 percent; Allergy initially probably covered 10 percent—of course, with the AIDS problem it covered more and more; and the Cancer Institute probably another 20 percent. These percentages probably add up to more than 100 percent, but those are the general dimensions.

NHLBI had by far the most extensive program in hematology, but the others played significant parts in the effort. So that was one of the goals that I hoped, if not to accomplish, then at least to get people thinking about.

Harden: Why was it that people throughout the community, both at the NIH and in the hematology community leadership, in general, were not very anxious to see an amalgamation take place?

Chernoff: I thought it a mistake to continue as a fragmented effort, but that is the way it was. That brings me back to my stay at NHLBI. After 10 years of leadership of the division, I considered my old philosophy that said it was time to move on and I retired from the NIH.

Harden: We will return to that phase of your career later.

Chernoff: I participated in two other activities during the period after I retired, or resigned, as Director of the Memorial Research Center at the University of Tennessee and as Director of DBDR. In 1975, I took an eighteen-month sabbatical from the University of Tennessee and became Medical Director of the Cystic Fibrosis

Foundation to try to help this private medically oriented public health foundation and interest group put its medical activities on a firmer scientific basis. By that I mean that the Foundation was an effective collector of money, able to influence Congress, but their orientation was largely social. They supported some clinical care activities but they did very little in the way of encouraging scientific research work. And, in that eighteen-month period, I believe I had a significant influence on turning the direction of the Foundation around. We published, with the support of a contract from the NIH, an extensive study of cystic fibrosis and published a five-year or ten-year plan that formed the basis of many of the activities that the Foundation became involved in in subsequent years. They helped sponsor research centers, they expanded their support for scientific training and scientific research and, just in the past two or three years, that support has paid off with the identification of the genetic defect in cystic fibrosis. While I did not have anything to do with the specifics of what emerged, I was able to contribute significantly to the Foundation's orientation and to how they thought about spending their money.

When I retired from the NIH, I took on a brief advisory consultative role at the American Association of Blood Banks [AABB], where I was given the official title of the Director for Scientific Affairs. I stayed there some two, two and a half years, helping the Association develop a somewhat more scientific orientation. I initiated and participated in the development of a five-year research plan and set up various think tanks that helped explore different areas of research for the future. That is a bird's eye view of my activities.

Rodrigues: One question about your efforts to try and coordinate hematology at the NIH. While you were unable to do this in a formal sense, were there any committees or other types of approaches that you tried to employ to coordinate activities?

Chernoff: We did a lot of talking among the various interested parties and I met with the leadership of the American Society of Hematology on many occasions to try to get them to think about the possibility of a more coordinated effort. As I indicated earlier, the leadership of the American Society of Hematology was adamantly opposed to bringing all the hematology work into one institute. First of all, I think they felt that they would fail in their efforts to get a separate institute of hematology or blood diseases; second, there was more loyalty on the part of the leadership of the American Society of Hematology to Arthritis and Metabolic Diseases than there was to NHLBI. They always seemed more supportive of Arthritis and Metabolic Diseases' efforts in Congress than they were of NHLBI's, even though they received the major part of their support from NHLBI. The Society's philosophy was based on the idea that it is better to have an egg in several different baskets. If something happened in the funding of one institute, they would be able to turn to another basket. It may be true theoretically, but I think it cost the Society heavily over the years in terms of the amount of support

and influence they could have had in general. So that was one of my losing battles at the NIH.

Harden: That could be the subject of another separate interview. We could explore the politics. I would like to discuss now when you first become aware of this new disease that came to be called AIDS. We have been told that there were conversations at hematology meetings about patients with immunological defects. We are talking about the period before 1981 when the first paper was published in *MMWR [Morbidity and Mortality Weekly Report]*. Do you remember when you first became aware that there was a new disease problem and what was being said about it?

Chernoff: I first became aware of the emerging problem in the summer of 1982, after the publication in *MMWR* of the first three cases of hemophiliacs who showed up with this disorder. Some hematologists, during the summer of 1982, indicated that they knew about other cases that were surfacing. [Dr.] Oscar Ratnoff was one, if my memory serves me correctly, who seemed to have had a sense of what was happening, but I do not recall ever hearing the problem discussed at formal meetings during that period. I heard about, but I was not invited to or involved in, a meeting between the National Hemophilia Foundation people and the CDC [Centers for Disease Control], and perhaps others, some time in the early part of the summer of 1982, but I have never seen any minutes of that meeting. Apparently, some initial discussions were held at it.

During the summer of 1982, there were additional rumors and occasional reports of more hemophiliacs coming down with ARC (AIDS-related complex). I cannot recall the specifics, but the reports were probably from friends and investigators at the CDC. [Dr.] Bruce Evatt was involved. This led me to call together, in September of 1982, an off-the-cuff, ad hoc group to try to help us deal with what we believed at that time was the use of clotting factor affecting hemophilia patients adversely or the existence of a defect in hemophilia patients that made them immunodeficient. I was never able to find any minutes of that meeting, but I do know that those attending urged us to support a small project that the CDC had in progress with the Hemophilia Foundation on immune changes in the hemophilia population receiving large quantities of blood products. We did provide, by an interagency agreement, a small amount of money to the CDC to carry out that study. I do not recall the amounts precisely, but it was not a major thing. It was within our ability to make these kinds of decisions more or less on the spur of the moment, with the concurrence of the director of NHLBI.

Harden: But this was definitely before the NIH interagency committee, [Dr. Robert] Bob Gordon's committee, was established and before that famous meeting in Atlanta and phase III.

Chernoff: Yes, I think it was in October of 1982 that we actually issued the interagency agreement and the NIH chronology on AIDS activities contains comments that NHLBI supported a study. I am sure that you have that chronology somewhere.

Harden: Yes. We have been putting together details from a variety of sources by going through various chronologies and files.

Rodrigues: We want to ask a few questions about the meeting in January 1983 that was called by the CDC. When we went through the records that we could find on the meeting, one of the things that confused us was that there seems to be a list of invitees that does not match the list of people who actually attended. Do you recall who attended from the NIH?

Chernoff: There were at least three of us who went to Atlanta on the morning of 4 January 1983. Bob Gordon, [Dr. Kenneth] Ken Sell, and I rode in a cab—I think it was a cab, maybe it was an NIH car—to the airport. From the airport, I believe there was at least one other person with us. I am sure that somebody from Allergy and Infectious Diseases, apart from Ken Sell, was there. It may have been [Dr. Anthony] Tony Fauci, but I do not remember who it was. The two that I was personally involved with were Bob Gordon and Ken Sell.

Harden: I remember that the three of you were all official designated representatives of the NIH. We came across some more people on a list at some point and we were not sure if they went to the meeting or not. Do you remember who they were?

Chernoff: My name did not appear on the very first list of invitees. It did appear on the list as an attendee at the actual conference.

Harden: Can you talk about the conference itself? There were many different constituencies present. You had the government with all its various subdivisions and you had the blood bankers, of which, if am correct, there are two groups, the voluntary blood banks and the commercial ones.

Chernoff: The latter are not blood banks. They are commercial plasma processors.

Harden: Right. But they have different interests, at least according to a couple of items we have read. At this time you knew that hemophiliacs were coming down with AIDS, and I believe there had been maybe one or two reports of suspected, if not proven, transfusion-associated AIDS. What was the concern and how do you recall that meeting?

Chernoff: A number of things had happened in the latter part of 1982. There was a meeting in early December of 1982 in which the Blood Products Advisory Committee of the FDA [Food and Drug Administration] was involved. At this meeting, co-

sponsored by the DBDR, some concerns about what was occurring in the hemophilia population were discussed. But the meeting in January 1983, in Atlanta, was promoted as an urgent effort to bring together people who were involved in different aspects of the problem of blood use and its possible role in immunodeficiency disorders. The idea was to bring these people, scientists, clinicians, blood bankers, and public health groups, up to date from an epidemiological and clinical standpoint and also to explore ways in which the blood banking community could address the problems that appeared to be developing. In addition, there was a tremendous amount of interest by other people wanting to attend this meeting, such as advocacy groups and the press.

As I recall, our plane was a little late coming in to Atlanta that morning and by the time we got to the CDC, probably ten minutes after the start of the meeting, the place was so jammed that we were sitting outside the main room on seats way in the back. The room was large and filled with people. I do not know how many were there, but I would guess at least two to three hundred people must have been crowded into that facility. A series of presentations, talks, was given. There was limited discussion in the morning, but in the afternoon hours, there was a lot of discussion. When the discussion turned to what the blood banking community should be doing, there was a sense that, while we had no clear idea of what was the root cause of the problem, it was necessary to initiate activities that would lead to a better understanding of what was happening. Though that was the philosophy, there was no consensus about what was the most appropriate thing to do. Differences of opinion existed at that point as no one knew unequivocally what the disease was caused by nor how it was spread.

It was difficult to start making meaningful procedural changes, not so much in industry, but in the medical approach to treating hemophilia on the basis of the limited amount of information that was available. Some people said that the evidence was just not there to suggest an infectious agent as the cause of the disease. Others discussed the possible role of nitrites in transmission of whatever caused AIDS, the possible role of excessive protein contact, and a variety of other theories that were prevalent at the time. A significant focus was on what was different about hemophiliacs that made them more susceptible to something that the rest of us did not react to.

An investigator from the CDC presented preliminary data on a variety of “surrogate tests” at that meeting. His name was Dr. Thomas Spira. Data were presented on blood tests taken from patients who had clinical AIDS, from some who had the ARC (AIDS-related complex), and also from some normals. The data were very preliminary. They showed that some of these tests, particularly the core antibody test, would have been positive in, let us say, a significant percentage of people who had AIDS and in a somewhat smaller percentage of people who did not have AIDS, but had evidence of ARC. The so-called normal

group also had a good number of positive tests, though less than in the other groups. Those data were presented as preliminary coming from a very specialized group of patients. They did not represent the usual blood bank donors. It was interesting that the presentors handed out the data on paper, but then collected the sheets, presumably because they did not want the data to get out of the room. The data were considered not to be verified at that point. So, although data were presented on a range of surrogate tests, there was no recommendation by anyone in charge as to the need to institute any specific test at this point.

The consensus at the meeting, or at least the feeling that I got out of the discussion, was that there was a need to do a lot of research quickly on these various tests. We needed to see if any of them, or any others that might be suggested, would be suitable for identifying people who appeared healthy but who might be carrying a presumptive agent for the AIDS disease, not those who already had AIDS, because the latter were not likely to be blood donors.

Harden: You have made a very important point in the sense of trying to recapture people's mindset at that time. Looking back, hindsight says why did everybody not recognize that the disease was caused by an infectious agent. What I mean is that the epidemiology was there, but, in fact, I suspect it was not clear. There were people who were saying that the causal agent has to be a virus. It was blood borne, it looked like it followed the hepatitis B pattern. But, as you said, there were a lot of alternative theories at this time. Could you say how you assessed the percentages of people in the room, in terms of who thought what?

Chernoff: I do not think there was an opportunity to evaluate that question within the small group with whom I dealt. However, there were largely blood bank people and experts in caring for hemophiliacs—people like [Drs.] Louis Aledort and Aaron Kellner and Joseph Bove—those are the ones that I talked to and who made their views known. There was real uncertainty about the implications of what was being presented. For one, some wondered whether the syndrome had anything to do with the use of factor concentrate or blood products in general. The blood bank people felt the data were not there to make a specific statement, or to take a stand, particularly one that was going to have such a profound effect on blood services and the availability of blood. So there were many comments about how little we knew about the disease and how uncertain we were about the situation. In the group with which I personally interacted, there was a feeling that we needed to do some carefully designed studies as quickly as possible in order to try to resolve the question. We had to define, first of all, or to identify, if possible, what was causing the problem and, second, to interdict the possible role of blood as being the vehicle for whatever was involved.

A number of developments emerged from that Atlanta meeting. For example, we convened a Blood Diseases and Resources Advisory Committee meeting in



January 1983 that urged our division to study the question of surrogate testing in relationship to AIDS. As a result of some of these discussions, [Dr. Edward] Ed Brandt, in the beginning of March, appointed NHLBI and DBDR as the lead agency and division in terms of research related to the development of surrogate tests applicable in the transfusion area. In part because of what the Advisory Committee did in January, we held on 15 March 1983 a very important meeting on the current status of the epidemic and the question of testing for it, co-sponsored, I believe, with the National Institute of Allergy and Infectious Diseases.

Subsequently, we developed rapidly a number of initiatives, one of which was an RFP [Request for Proposals] for a contract on the subject "Association of Blood Product Use with Immune Function Changes: Relation to AIDS." In addition, an RFA [Request for Applications] focused its attention on "Assay Methods to Detect the Carrier State of AIDS." The latter moved rapidly through the institute's review process so that we had it on the street by the middle of July after clearing Claude Lenfant's office and our two advisory committees, first, the Blood Diseases Advisory Committee and then, the NHLBI Advisory Council. That whole process, from our being designated the agency responsible for this area in the beginning of March to the actual appearance on the street of this RFA, was no more than a matter of three months, which is very fast at the NIH. We received applications in October and awarded them the following February. Thus it took less than a year between the initial emergence of the RFA to the funding of the grants, which, again at the NIH, is pretty fast.

To make a long story short, throughout that period of time, even as late as February of 1984 when the RFA was funded, but before the virus had been identified, there was still uncertainty as to: (a) what caused the disease; (b) what specific roles transfusion and blood products were playing. Needless to say, two things were happening: first, there was an increasing sense of urgency on the part of those of us who had anything to do with blood and blood product use; and second, that we had to assume the worst and plan our strategy on the basis that a transmissible agent was involved. While the majority of the people in the transfusion area did not feel that there was enough evidence to prove that a transmissible agent was the cause of AIDS, that feeling began to decrease toward the end of the summer of 1983. By the end of 1983, most people in the transfusion area felt that there must be a transmissible agent involved.

The question concerning a causative agent was still an open one in February of 1984 when we awarded approximately two million dollars worth of grants to study surrogate tests capable of identifying potential carriers of the disease. When the announcement of the discovery of the causative agent of AIDS was made six or eight weeks later, we went back to our awardees and requested that, with the virus having been identified, they should shift the emphasis in their RFA

activities, if possible, into more specific tests to identify the virus. That was the sequence of events, at least from my recollection.

Rodrigues: Within the Heart Institute, specifically in your division, it was not clear to me from what I have read as to what other components of the PHS [Public Health Service] were also involved with blood safety issues. The CDC called this meeting in January 1983, but which component of the CDC had the lead on transfusion concerns.

Chernoff: I do not know the CDC part very well. Bruce Evatt at the CDC was the person who was most involved with hemophiliacs and the National Hemophilia Foundation activities and was closest to us, but we also dealt with [Dr. James] Jim Allen and [Dr. James] Jim Curran.

Harden: What about the FDA? The same question.

Chernoff: I do not know who was responsible at the FDA, possibly [Dr.] Dennis Donohue or [Dr.] Paul Parkman, but there was a lot of interaction between them and our division. We met jointly in various environments and in various venues. We had many discussions with the staff of the FDA because of our mutual interest in hepatitis and hepatitis testing. The transfusion transmitted virus study, which had been ongoing for a number of years, involved not only the NIH but also the FDA. We invited FDA scientists to our discussions and our meetings and they often invited us to theirs. We co-sponsored the FDA's Blood Products Advisory Committee meeting in December of 1982. Similarly, in December of 1983, we co-sponsored the very important Blood Products Advisory Committee meeting [BPAC] on surrogate testing. Dennis Donohue and I gave the introductory remarks at that meeting, and while we did not have an active role in the presentations, we were certainly involved in what was going on.

Harden: As this was December 1983, it was before the virus was found. What was the major point of discussion? Was it the hepatitis B core antigen that was being recommended?

Chernoff: About ten different people made presentations. [Dr.] Joanna Pindyke reported on studies from the New York Blood Center and [Dr. Herbert] Herb Perkins presented studies from the Irwin Memorial Laboratory on the West Coast. [Dr. Ronald] Ron Gilcher talked about studies in the Midwest. Dr. Spira, who spoke at the 4 January 1983 CDC meeting, presented data at the December 1983 Blood Products Advisory Committee meeting on potential surrogate tests which were different than the ones he mentioned in January. In January, he talked about core antibodies, about immune complexes and certain hepatitis studies that they were doing. In December, he offered studies on a urinary protein called neopterin which he found to be even more specific for picking out people who were AIDS

and ARC type individuals. Several people at the meeting focused on the use of core antibody testing as a surrogate test. Many different suggestions were made at the December BPAC meeting but, again, there was no consensus reached.

It was very interesting that Herb Perkins presented data at that meeting on his so-called zip code study. He compared core antibody tests in zip code areas of San Francisco that had very low numbers of homosexual people versus other areas with high numbers. He found that the percentage of people with positive core antibody tests, for example, was just as high or higher in areas with low numbers of homosexuals as it was in those areas with high numbers of homosexuals. Other reports also cast some doubt on the specificity of the core antibody test for identifying potential carriers of a presumed transmissible agent.

Harden: What was your feeling?

Chernoff: My feeling was that we had to assume that there was a transmissible agent involved, but I did not think any of the tests that were being proposed at that point gave sufficient discrimination between those who carry what we later knew was the virus compared to those that did not.

Harden: This is a hypothetical question, but what would you have said to a family member or close friend who called at that time and said, "I need to have surgery. What should I do about the blood supply?"

Chernoff: I am not sure of how I would have responded. Probably I would have said, "If you can get away without using blood in surgery, don't use it. If you were in San Francisco, or Los Angeles, or Miami, or New York, which were the four cities with the highest number of cases, I would be very hesitant about taking blood. But, most important, if you don't need it, if you can get away without it, get a surgeon who will deal with you without using blood." It is a little hard to be sure what I would have said because I know a lot more now than I did then.

Rodrigues: In one of the articles that I read on this general subject, the author suggested that throughout the sixties and seventies the way clinicians prescribed the use of blood was incautious, that it had become almost a convenience. The author later suggested that AIDS may have actually had some beneficial side effects in terms of getting people to be more discriminating, particularly in the use of whole blood. What would be your perspective on that kind of observation about the trends in the use of blood and the emphasis on other techniques or other ways of avoiding the use of blood?

Chernoff: I mentioned earlier that I was not a blood banker. I did not focus on transfusion medicine until I got to the NIH and there I became rapidly involved in all aspects of the subject. I came to the NIH in 1978. By late 1979 or the beginning of 1980,

I probably felt that blood was being overused; that most single unit transfusions were probably not necessary. If patients could get along with just one unit of blood, the majority of them probably did not need any.

I also felt that education of physicians in the proper use of blood was something that ought to be encouraged. If you look at our division's various annual plans, in the transfusion area we stress the need to educate physicians in how and when to use these materials. As time went by, in the early 1980s, we developed such an educational program, which came to be known as the Transfusion Medicine Academic Award, one of the main aspects of which was to educate physicians and medical students in the proper use of blood and blood products. Incidentally, at that time, the blood resources part of the NIH began to be known as the transfusion medicine department. I am afraid I have strayed a little, but have forgotten what your original question was.

Rodrigues: My question had to do with the impact that AIDS had on the whole field of transfusion medicine in terms of promoting salvage techniques and alternatives.

Chernoff: As I have already stated, we had already begun to promote the idea, before AIDS came on the scene, that better education in the use of blood and blood products was necessary. Blood use was increasing much more rapidly than it needed to be, even considering the changing therapeutic approaches being introduced for a number of medical and surgical conditions. When AIDS came on the scene, particularly by 1984, it was obvious that there was yet another reason to limit the use of blood. Hepatitis was recognized as an important consideration in transfusion medicine long before AIDS. Data from the late 1970s showed that approximately 3 percent of transfusions were transmitting hepatitis and that the average patient who got blood received approximately 3 to 4 units of blood during a hospital stay. Thus, his or her chance of getting hepatitis from a transfusion as a result of a hospital stay was about 7 percent, which is a very sizable risk. Long before the HIV virus appeared, blood bankers were concerned about the use of blood in questionable circumstances because of its ability to transmit other diseases. And that feeling, I think, became stronger as time went by. Certainly, the onset of the HIV virus made it extremely important to modify and moderate the way that blood was used in the clinical setting.

Harden: I have been struck me by how long it took before the full picture of AIDS emerged, that indeed if you got the virus, it might be ten years later before you got the disease. It is 1987 and 1988 before even these facts are shown definitely.

Chernoff: There were three studies relevant to that question. In the mid 1970s, NHLBI and DBDR supported the TTV study. This was the transfusion transmitted virus study that established the 3 percent level I referred to previously. It established the fact that hepatitis was a lot more common than people had anticipated and that the

study of ALT levels was one way of being able to exclude possible infectious units. That study went on into the late 1970s and early 1980s. It established the so called non-A, non-B hepatitis, as a significant part of the transfusion transmitted hepatitis problem.

When AIDS came into the picture in late 1982 and 1983, we began to support similar studies focusing on the AIDS problem. The first thing we did was the RFA to study surrogate tests, which, you remember, was our mandated responsibility according to [Dr. Edward] Brandt's directive in early March. A second thing that we started was the so-called transfusion safety study [TSS], which had as its goal an understanding of the effect of multiple transfusions in a variety of diseases. Transfusion itself was implicated as being a potentially unsafe procedure. People who had many transfusions had their immune systems affected whether they had viruses or not. The transfusion safety study was aimed at looking at some of these questions. It focused its efforts in areas of both high and low AIDS incidence and involved people who received transfusions for thalassemia, sickle cell disease, heart disease, and so forth. A separately funded part of that study was to collect blood specimens from two hundred thousand donors from October of 1984 till January or February of 1985 (before the test for HIV was commercially available and certified for use in blood banks by the FDA, which did not occur until later in 1985), and to put those specimens into a repository for later testing after the HIV test was approved. Of course, this would have occurred after the blood had been used, but would have allowed investigators to follow what happened to the recipients of that blood.

To summarize, these three activities provided important information in our understanding of what was happening. The TTV study established the mechanism for doing meaningful clinical studies in the transfusion field. It helped identify non-A, non-B hepatitis as a major problem. It was a study that Wolf Zuelzer was very much involved in initiating and I became involved only at the tail end of it. Then there was the RFA to study surrogate tests, specifically, and the transfusion safety study which was designed to look at the role of transfusion as a factor in the genesis of post-transfusion disease. These were three distinct but important studies in this whole process.

Harden: It is very good to have that clarified.

Rodrigues: Within the Heart Institute, would you say that most of the AIDS activities were centered in your division or were there other components of NHLBI that were working on the disease?

Chernoff: Initially, it was hard to sell the administration at NHLBI on the importance of this overall effort. We did manage, however, to convince Dr. Claude Lenfant [Director, NHLBI] that it was an area of importance for our institute and

eventually he accepted our recommendations. There was some reluctance, as I remember it, on the part of Claude and his staff, initially, to support the costly programs needed. But when Brandt's directive came out, I believe Claude recognized both the medical significance and the political value of having a prominent role in this area and so he became much more receptive to the idea. But we had a hard time pushing the 25-million dollar contract proposal through his office in the beginning.

We were the only ones in NHLBI who did anything related to AIDS for the first year of the epidemic. All the creative juices, if you will, came from DBDR's staff. We initiated efforts to hold meetings, we got people together, and we represented the NIH in different venues. For almost eight months, we tried to develop an ad hoc advisory committee dealing with AIDS and the role of transfusion. We were unsuccessful, not because our NHLBI administration was against it, but because the CDC did not want to have such a group, as they felt that they already had a committee looking at transfusion-related AIDS cases. But, eventually in January of 1984, we had our AIDS working group put together. [Dr.] June Osborn was the first chairperson of that group and she subsequently became the chair of President Reagan's AIDS commission. We got her started in the AIDS field.

Harden: Was that within NHLBI?

Chernoff: That was within NHLBI.

Harden: There was not any intramural NHLBI research on AIDS that you know of?

Chernoff: Well, there were the studies that [Dr.] Harvey Alter was carrying out, in part with NHLBI support, but he was not NHLBI.

Harden: He was at the Clinical Center, I believe.

Chernoff: Yes. We supported some of the Clinical Center's work through interagency agreements such as Alter's studies on the use of chimpanzees to determine the potential infectivity of AIDS patients' plasma. We also supported a chimpanzee colony in Texas to provide the animals for his studies. We helped the CDC through interagency agreements on several transfusion-related studies, as I have already discussed. We also finally developed the DBDR ad hoc advisory committee on transfusion-related AIDS, on which there were representatives of the CDC, the FDA, the Institute of Allergy and Infectious Diseases, and a variety of other governmentally related agencies. We included representatives of the National Hemophilia Foundation, the American Red Cross, the AABB, and the American Society of Hematology among others. But, basically, it was a committee that provided guidance to the DBDR. After meeting for about a year,

the group became the NHLBI committee on AIDS.

Harden: Was there any effort to support further research on the development of blood substitutes?

Chernoff: That effort had been going on for a long time.

Harden: Did AIDS have any impact on that work?

Chernoff: It did not have a direct impact because there was already a program on blood substitutes in place dating back to the late 1970s, even before I got to the NIH, and it continued. DBDR supported the perfluorochemical studies for a long time and some of them may continue even today. With the advent of AIDS, there was a new urgency about the effort. Nothing specific was changed other than to encourage investigators to submit new proposals. We had trouble getting investigators in the scientific community to focus on transfusion-related problems since their applications tended to fare so poorly at the study section level.

The Hematology Study Section was not attuned to transfusion-related problems. The blood bankers felt that they were not getting a decent or fair evaluation of their proposals from a group of study section members who were more attuned to supporting cutting edge, basic science studies of such subjects as genetics and immunology. Transfusion medicine problems were looked at as more practical kinds of research. Unfortunately, there were not enough skilled investigators submitting applications in this area. It was kind of a vicious circle. If you have a group that is sympathetic, you get more applications. If you have a tough group that is not really oriented to transfusion medicine, you tend to discourage people from applying. Then the problem becomes one where you do not have enough applications to justify a dedicated study section for transfusion medicine. That has been a problem at the NIH for a long time for the transfusion medicine community.

In the beginning of my ten years at NHLBI, about 80 percent of the studies supported by the Blood Resources Branch were under contracts. By the time I left, probably only 40 percent were supported by contracts and the rest were in the investigator initiated arena. But investigators always seemed to have difficulty in gaining support at the NIH, not specifically at NHLBI, but throughout the institutes because of the presumed reluctance on the part of study sections to give high priorities to studies that were less basic in their orientation.

Harden: Very interesting.

Rodrigues: Were there any ties with any other countries in terms of transfusion medicine at this point? At any of these meetings, were there representatives from other

countries?

Chernoff: There were representatives from, and to, other countries. I was the NIH representative on the Council of Europe's Expert Committee on Blood Transfusion during my years at the NIH. At their meetings, I presented the first few reports on the emerging problem of AIDS and transfusion medicine. I was, in a way, the original conduit of information about what was going on at the NIH and what I knew about AIDS in terms of the hemophilia population. This committee was like the FDA in this country. It was an FDA-like structure of the twenty-one member nations of the Council of Europe.

I lectured in Scotland, France, Germany and other places in Europe about transfusion medicine and the AIDS situation. I may have been the first scientist to brief the transfusion community in the Soviet Union, which denied that it had any cases at all, on the unfolding situation. But, in any event, I was one of the earliest scientists to present formal lectures about what was going on in the U.S.A. at these various international meetings.

In addition to these interactions, we always tried to involve foreign countries by having their representatives communicate with us. The Soviet delegation came several times to this country and spent time with us and with [Dr.] Aaron Kellner at the New York Blood Center, as well as with [Dr.] Harvey Klein at the blood bank at the NIH. We also encouraged foreign scientists to submit applications for our RFA, and there was one applicant from Spain that we wanted to support as part of the TSS contract but we encountered some roadblocks on doing so with a foreign national. I believe that we also did not get as much money as we needed to add foreign investigators to the contract. Those were the days when you still had to argue about getting money to support an expensive contract, even if it involved AIDS. Yes, there were many interactions with foreign countries.

Harden: Now, we have the major outlines. What else should we discuss?

Chernoff: There were numerous meetings during 1983, almost weekly and in some periods more than weekly. There were telephone conferences. There were special transfusion reports. I remember how we congregated in the offices at the FDA around a speaker phone, and interacted with people from the FDA, the CDC, our institute, and others for a weekly report on what was happening epidemiologically and what new transfusion related cases were being discovered. So there were a lot of meetings. Jim Wyngaarden set up an NIH-wide AIDS working group, and I was NHLBI's representative on that committee. I told you about our AIDS advisory committee—the ad hoc group which June Osborn chaired—that started in January 1984. We held several other formal meetings during the course of 1983—one in September that was focused on epidemiology and surrogate testing; the BPAC meeting in December that focused on surrogate testing and the core



antibody test. We were probably in meetings at least once, if not two or three times a week during that period; most of them were not formal meetings and so no minutes were kept but there was a lot of effort made to keep channels of information flowing. And, finally, I and others appeared before congressional committees during the summer of 1983 to discuss the roles of our various agencies in fighting the disease.

I was also involved in a number of other meetings for which the Hemophilia Foundation was the primary initiator. There was a meeting in January 1983 in New York which I had attended but of which I have very little recollection. The AABB and the American Red Cross organizations also sponsored meetings in which DBDR was involved. Likewise, ABRA, the American Blood Resources Association, which is the overall group of the plasma people, had meetings at which we presented information. And let us not forget the American Blood Commission on which DBDR served as an active member. Yes, there were meetings all over the place.

Harden: That was in 1983 and 1984 and then, once there was a virus agreed upon, did meetings become more focused?

Chernoff: Our efforts became much more focused at that point.

Rodrigues: I saw a few references in the files we were going through that mentioned the NHLBI AIDS working group. But other than the information that the group existed, I have never found anything else about it. I do not know how long it existed.

Chernoff: Another group I should mention is the Interagency Technical Committee of NHLBI. [Dr. David] Dave Robertson and I were co-chairmen of the working group on blood resources. In any event, the first brief recorded mention of AIDS comes in the summary of this group's meeting on 28 September 1982.

The June Osborn ad hoc committee, which began in January of 1984, became, in reality, the institute's advisory body by the end of that year. As I mentioned before, no formal minutes were kept, though I have some notes of what was discussed at several of the sessions. The NIH AIDS committee was created during 1983 and continued for several years under Bob Gordon's chairmanship.

Rodrigues: We have had, I guess you might say, spotty results in getting records. Some offices are very good in keeping their files and other offices tend to purge things very quickly.

Chernoff: Unfortunately, my secretary threw out all of my files after I retired.

- Rodrigues: I know when I went to try and get some of Dr. Richard Krause's records practically everything that they had from the late 1970s and the early 1980s was just gone.
- Chernoff: I have the CDC summary minutes of that 4 January 1983 meeting in Atlanta. As you see, Tony Fauci, Jim Goedert, and Ken Sell were all present. Sell, Gordon, and I appeared on the actual attendees' list, and I know others were there as well. As I said a moment ago, that the first mention of AIDS at an NHLBI function appeared in this 28 September IATC meeting and it is just a brief mention in one paragraph. I have a copy of the first memo that Claude Lenfant ever wrote about our activities. It talks about the conference that we wanted to hold in March of 1983, and that we would be a part of another conference in April. Also I have Jim Wyngaarden's authorization, giving us responsibility for transfusion AIDS studies.
- Rodrigues: That is interesting because I am almost certain that this did not appear in the Office of the Director files or, if it did, it is now gone.
- Harden: Wasn't there quite a scandal at some point about local blood being contaminated and why the Red Cross was not staying on top of the problem? A second question is about the scandal in France after which people went to prison because of problems in the blood supply. Do you have any comments on what happened and how it all managed to go wrong in both circumstances?
- Chernoff: I do not know the specifics of the Red Cross problem that you just mentioned. I have opinions about the French situation, but they are based more on what I read in the newspaper and on what I recall about the events themselves. In the French litigation, I believe the individuals being prosecuted, who have been convicted at this point, are taking the fall for a government decision to promote French development and French industry. It was a conscious decision on the part of the French ruling parties at that time not to let developments from outside the country interfere with internal French developments. I think the people who were convicted, without knowing anything more about it than what I read in the newspaper, are taking the fall for a public policy position that the government is mainly responsible for.
- Harden: Were you aware of the French blood test for AIDS that was competing for patent rights with the blood test developed by Dr. [Robert] Gallo's laboratory. You know the brouhaha surrounding that, but were you aware of any differences in the quality, the sensitivity, for example, of the blood test that the French were proposing.
- Chernoff: I have no direct knowledge. I understand that the French test was not nearly as specific as the American test and that the quality control on it was nowhere near

equivalent.

Harden: There was not a lot of discussion about it that you recall.

Chernoff: There may have been in some circles but not in ours.

Harden: Well, I believe the effort to talk with people involved with the NIH response to AIDS is worthwhile, because otherwise a lot of material would be lost. We are most appreciative and we thank you for talking to us today.