

*This is an interview with Dr. Richard Krause at the National Institutes of Health (NIH), in Bethesda, Maryland, 17 November 1988. Dr. Krause was the former Director of the National Institute of Allergy and Infectious Diseases (NIAID). The interviewer is Dr. Victoria A. Harden, Director of the NIH Historical Office.*

Harden: Dr. Krause, would you summarize your career before 1981, when AIDS was identified, and perhaps indicate your areas of special interest and research? How do you think these might have helped prepare you for encountering this disease?

Krause: After medical school I was trained in internal medicine at Barnes Hospital in St. Louis. Before that, during medical school, I took eighteen months off and worked with the late Dr. Charles H. Rammelkamp of Case Western Reserve University School of Medicine. He was working on the prevention of rheumatic fever by early treatment of streptococcal sore throat with penicillin. There was an argument at the time as to whether treatment would prevent subsequent rheumatic fever. This was between 1948 and 1950. "Rammel," as we called him, was convinced that rheumatic fever could be prevented, but most people at that time disagreed with him. A long series of clinical and epidemiological studies by Rammel and his group proved without question that this could be done. They received the Lasker Group Award for this work.

It was great fun to be associated with Rammel and this clinical epidemiological research, in which the laboratory, the clinic, and the fieldwork were all a unit. Some believed then, and some do even today, that epidemiology should be pure and not be contaminated with laboratory work or clinical work. I think this early experience really prepared me for the position of director of NIAID and for the AIDS epidemic.

Also, for a period of about four months during World War II, I worked in a venereal disease control program in the U.S. Army. I was an enlisted man at the time with no medical training. I remember very well the sexually transmitted diseases (STDs) control programs and the measures that were taken. Many of these have been advocated in the 1980s for the prevention of the transmission of AIDS and STDs.

After graduation from medical school and two years of training in internal medicine at Barnes Hospital, I went to Rockefeller University from 1954 to 1975. There I did clinical investigation on patients with rheumatic fever, but most of my research was concerned with immune response to streptococcal antigens. I made the discovery in the early sixties that immunized rabbits produced antibodies of remarkable molecular uniformity and in large quantities. This was before monoclonal antibodies had been prepared by Dr. Cesar Milstein and Dr. Georges Köhler. Therefore, from 1965 until 1976, our work was a very useful source of homogeneous antibodies, either for structural studies on antibodies or as probes

for research in immunogenetics. A great deal was done on the genetics of the immune response using these antibodies particularly by my former associates, Dr. Thomas Kindt, the laboratory chief at NIAID, Dr. Klaus Eichmann, Director of the Max Planck Institute of Immunology, Freiburg, and Dr. Dietnam Braun, Ciba-Geigy, Basel.

I came into the directorship of NIAID therefore, with a broad background in microbiology and immunology, and with an interest in clinical medicine and clinical epidemiology. Because of my background, when I was appointed director, the microbiologists thought that I was a microbiologist and the immunologists thought that I was an immunologist. Both groups were disappointed, because after a year or two, I supported both camps and not one or the other. There is nothing you can do about that.

One of the first things that happened after I joined the government was the "swine flu affair," which occurred during the winter of 1975-76. Several young men died at Fort Dix of a strain of swine flu virus thought to be related to the virus that caused the pandemic of 1918. There were approximately five hundred young men who were infected, but this was a mild infection, except for the one or two deaths.

There is no point in reviewing that whole history in detail. On the basis of a few cases, we put on a major effort to develop the swine flu vaccine and prepared to immunize the population. The experts all agreed that it was the only thing to do, and I think that most would make the same decision today, given the same set of facts. The pandemic of World War I hung over our decision. We knew that vaccination was the only way to get ahead of an epidemic, since influenza often begins in one season and then bursts into the next. So we went ahead, made vaccine, and immunized forty million people. Influenza did not occur the following season. After that we had a change of administrations.

Mr. Joseph Califano came in as the Secretary of HHS [Department of Health and Human Services]. There was a good deal of second guessing about the swine flu effort. It is not clear to me how I could have played a different role one way or the other. But that left an impression on me--committing major resources to a potential problem, which afflicted only a few. The cause of these people's deaths was an unexpected strain of flu. As a result, there was an incredible mobilization, and this led to serious repercussions.

Would I, along with the others have made a different decision? Probably not. But in retrospect, maybe rather than use it, we should have stockpiled the vaccine until we were certain about the possibility of an epidemic. However, experts like Dr. Albert Sabin said at that time, about February or March of 1976, that if we did not immunize the children before they went to school in September, we would not stop the epidemic. This is because flu spreads after the children are brought

together, and once it starts spreading in the schools, it is transmitted to the families. I remember that from the meeting in the White House cabinet room with President Gerald Ford. The consensus of the group was to vaccinate early, not just to stockpile the vaccine.

Another episode sensitized me to the political reaction to commitment of resources to the treatment of less common illnesses. An NIAID achievement, when I came on board, was the use of pure bee and wasp venom for desensitizing patients who were at risk of fatal anaphylaxis after a sting. This was a major advance, because before that time, desensitization was not very successful. [Dr. Lawrence M.] Lichtenstein at Johns Hopkins [University] developed a desensitization method using pure venom. It worked beautifully. Sensitive people can die from bee or wasp stings, particularly people who work outdoors, surveyors, engineers, telephone linemen ...farmers. Once you have successfully desensitized the person who is in danger of fatal anaphylaxis, no reaction occurs when such people are deliberately stung by a wasp in the clinical laboratory. So that was very impressive.

The point is this. When we go before the appropriations committees of Congress, we must describe achievements of the previous year. Senator [Thomas] Eagleton was in the chair and asked about new advances, or something to that effect; you can find it in the record. (The records of congressional testimony would be a useful place to find what Dr. Vincent De Vita and I said about AIDS in the 1980s.) So I explained what we had done about bee stings. I could see that Senator Eagleton was not impressed. I could see it in his face. He asked, "Dr. Krause, how many people die each year of bee and wasp stings?" I said perhaps fifty, perhaps 100. He replied that that was of course unfortunate, but I could see he did not consider this a major health issue. For all I know it could be 500 or 1,000 people. Certainly it is not a large number. On the other hand, there are many, many thousands of people who live in fear of death, because they know what a severe reaction they can have, and they are appreciative of this medical advance.

Nevertheless, that episode sensitized me to being evenhanded in the use of scarce resources for a smaller number of patients. Of course, they are important. But there were many problems, many demands from 1975 to 1985, and the NIAID was stretched very, very thin. For years it had the lowest pay line (the percentage of approved grants paid) of all the institutes. Too many scientists thought infections were no longer important and that view was translated into a decision in NIAID's budget.

When I took over as Director of NIAID, Dr. Lewis Thomas said, and even Dr. Don [Donald] Fredrickson said, "Now that we've conquered infectious diseases, and we don't have to worry about them any longer, we'll worry about heart disease

and cancer and so forth." Lew Thomas has since taken that back. I wrote him a letter saying, "I'm delighted you've rejoined the Mother Church, it has been very lonely here on the front line with everybody having deserted us." He wrote a charming note, "I never left the Mother Church. I was over in a quiet corner praying before the candles for the diseases we do not know about, such as kuru."

That was the picture when AIDS occurred. NIAID was spread very thin, a little bit like the Confederate forces during the Civil War, and we had to be selective in what we did. We could not put our fingers in every leak in the dyke. As important as small numbers of patients are, with limited resources, we had to be selective. When push came to shove, rightly or wrongly, I usually made the decisions for broad-based biomedical research, because the fundamental answers to immunological diseases and virus infections were going to take a lot more research to understand; for example, how to treat immunologic and virus diseases and how to prevent them. There is no penicillin for virus infections. So, in general, when push came to shove, I was on the side of substantial support for basic research and as much applied research as we could afford. And we could not afford as much as NCI [National Cancer Institute] or NHLBI [National Heart, Lung and Blood Institute] could.

And yet, if we were to receive an increase in the budget resources from the administration and Congress, we had to make a case for it in the disease arena. It is very hard to sell basic research alone.

So in the 1970s, from 1975 to 1980, I organized a series of task forces on virus infections, on immunologic diseases, on sexually transmitted diseases, and on asthma and allergic diseases. A lot of work was done by the extramural and the intramural scientists to produce the reports of these task forces. They produced guiding principles for the priorities of the institute on what was needed in basic research and clinical research. This was all done just before the AIDS epidemic struck. Between 1975 and 1980, the NIAID budget increased by 100 percent. So we were beginning to have an impact.

During that time, the staffers on the Hill were pushing us to do something, to get the word out to the public, about herpes, etc., and so we did. We brought out a very good movie called Jennifer: The Revealing Story of Genital Herpes. You may want to see it sometime. It is a very good movie, and it was very well done. So we were very much involved in the STD business, and I pushed this. It was one of our special programs. It was something that I knew was a serious problem because of my days in World War II. I was sensitized to it. During wartime you have societal changes, resulting in the same sort of thing as the sexual revolution of the sixties and seventies, but for different reasons. Certainly during wartime you have a change in mores.

Harden: I would like to come back to that later, about comparing other STDs and AIDS.

Krause: Right. To inform the public I wrote a book on the fact that infections were not going to go away. It only takes twenty-four hours for an epoch to come and go in the microbial world. Microbes reproduce every thirty minutes. We reproduce every twenty years; therefore, a season to us is a millennium for them. They can come and go in a season. We do not come and go that fast. That means that they have a tremendous genetic advantage over us, and always will have. They were here, on earth, for two billion years before we arrived, and they are going to be here for probably two billion years after we are gone. In any event, this ebb and flow of microbes and humans I put into a book titled The Restless Tide. I do not know whether you have seen it. Margaret McElwain, the information officer at NIAID, worked on this with me. I dedicated the book to her. She died in 1978, which put me back a bit, but then I finished it with Nancy Brun's help. It was all ready to go to press in 1980, when we had some arguments with various publishers, and nothing was done until March 1982, when it finally came out. By that time there had already been the first AIDS report in 1981.

I did not mention AIDS in the book, but the book was reviewed in the national gay newspaper, the Advocate. I think it was Nathan Fain who did the health reporting in the Advocate. I did read the Advocate from time to time to read his health articles, particularly since he was writing in the Advocate about AIDS. He was one of the early people who talked about behavior modification. In his review, he referred to me as the man who predicted the AIDS epidemic. I did not predict AIDS, but I did predict we would not see an end of infection as the cause of human misery. That pretty much brings this history up to where I was prepared to worry about AIDS.

Harden: All right. Let us look back and think in terms of diseases striking the human population--for example, when syphilis hit in the early sixteenth century. In Europe, it was a very deadly disease, and something that could not be dealt with easily, like another disease—the bubonic plague. When a disease that we do not understand strikes a society, it can cause great panic. Do you think more panic might have resulted from AIDS if it had hit us in 1955, before we knew about B-cells, T-cells, and retrovirology?

Krause: There is no doubt, as others have commented, that if AIDS had to strike, we were prepared because of the research advances between 1950 and 1981. We are a long way from a vaccine, although I hesitate to make a prediction like that, because something may come out of the woodwork in another year or so. Finding a drug to treat any virus infection has been tough, but it is not impossible. It has been done before. We have amantadine and rimantadine to treat flu. And, acyclovir is effective in the treatment of herpes. It does not cure the latent infection, but it has made a big difference in the treatment of the herpetic lesions. There are a few

other antiviral drugs, but not many. Developing antivirals is not like developing antibiotics for bacteria. It is tougher, due to the nature of the virus infection process that is so intimately associated with cellular mechanisms of the human host.

We were certainly much, much better prepared for AIDS in 1981 than we would have been, had it occurred in the 1950s. Yet we would have made some advances even then. The principles for identifying sexual transmission of a disease were in place. We already knew about retroviruses. Rous sarcoma virus is a retrovirus. We knew about latent virus infections, so I think that, although we would not have understood all the intricate details, we would have used other methodologies rather than T4-T8 ratios and things of that sort to measure the immune abnormalities. Now we use a much more sophisticated approach, but I am not so sure we would have been entirely in the dark because we did not have the same methods that we have today. We would have used cruder immunologic techniques to make a diagnosis. After all, diagnosis of AIDS is still somewhat fuzzy clinically, the immunologic alterations, precise identification of the virus, its presence in the cells, the detection of anti-AIDS virus, the antibody. It would have taken us longer in 1950 to come up with a serological test. We did not have the ELISA [Enzyme-Linked Immunosorbent Assay] in those days. We did not have the radioimmunoassays. We did not have Western blots. We did not have the polymerase chain reaction [PCR] before 1986. Therefore, we had fewer and less sensitive serological tests. On the other hand, we would have lived with that because we had lived with the Wassermann test as the best test for syphilis (at best, 90 percent accurate).

I grew up in an age when we knew our laboratory tests were never 100 percent accurate, and you always took that into consideration. Today everybody wants a test to be absolutely accurate. But a test must always be used within the clinical context. A 1950s serological diagnostic test would have been somewhat more primitive, but I think we would have come up with something.

We would have been way behind in not knowing enough immunology or virology to come up with an antiviral drug or vaccine, if possible, for two reasons. First, we have had thirty years to gather a lot of basic information about virology and immunology. Secondly, there is now new technology. We could not sequence a protein or a nucleic acid then. None of that could be done. All of that technology is currently being used to develop drugs and vaccines for AIDS. This is rambling answer to your question.

Harden: No, it is a very good answer. Now, let us go back to 1981-82. Can you recall when you first heard about these unusual cases and how your own thinking about AIDS developed?

Krause: I do not remember the exact circumstances. I cannot remember now, although Dr. [Jack] Whitescarver or Dr. [Kenneth] Sell might remember. I do not remember whether or not I heard about these cases prior to the publication of the paper. I probably did, because I scanned the CDC weekly Morbidity and Mortality Report. There are always a few cases occurring here and there of this or that that get reported. Some are quite a puzzle for a while, but then the mystery gets cleared up. They get investigated by the CDC, and it turns out that these often get written up in The New Yorker because they are interesting epidemiologic success stories. In one episode recently, they found that several hundred people in Iowa were wasting away unknowingly because the jowls of pigs or cattle, which contain a lot of thyroid gland, were being used in cheap hamburgers that were consumed locally. The patients were suffering an "epidemic" of hyperthyroidism because they were eating the hamburgers rare, and the thyroid hormone was still active. The solution was to cook the hamburger thoroughly. These things get investigated and solved. These episodes are interesting and brought to one's attention by the CDC and are soon usually under control. I suspect that was my reaction to the first report of a few AIDS cases.

Later on, I remember hearing about Kaposi's sarcoma, and saying to myself, "Well, if it is Kaposi's sarcoma, it is Cancer's [National Cancer Institute] problem, because we [NIAID] have enough to do." The CDC was doing the epidemiology. So I thought a very few cases of some sort of cancer were occurring. There was discussion at the time about the cause; by drugs, or by a combination of drugs and other virus infections that the patients had. We did not know if cytomegalovirus, hepatitis B, and other viruses resulted in some alteration that made the patients susceptible to these sarcomas.

You might say that, at a closer look, a sensible person would have recognized that it was an NIAID responsibility, also, because it was occurring among men who were very active sexually, and therefore AIDS should be an STD until proven otherwise. So I am prepared to take any blame for not immediately assuming that it was an STD. In retrospect, it was a disease of a sexually active group of people. Also, people of that age group do not usually get chronic diseases. In people of that age group, if they get a disease, it is usually infectious, unless, of course, the patient is the rare case who does get cancer, have a heart attack, and so forth. If there is a cluster of cases, one probably ought to think of a common source (infection, toxin, etc.), but then again, this is in retrospect.

When it was reported by the CDC that AIDS was sexually transmitted, I said, "Okay, it is in our ballpark, and we have to do all we can do." I cannot remember the exact date when that was. About six months to nine months after the publication in the New England Journal of Medicine of the first cases, the CDC showed a diagram of a dozen or more transmitted cases on the West coast and on the East coast from one sexual partner with AIDS. That must have come out in

about 1982, and then we began to gear up. Dr. Tony [Anthony] Fauci and Dr. Kenneth Sell were interested in the immunology side, and we alerted our STD centers to get involved, and they did.

One of the things that I had said to Randy Shilts, and to anybody else who would listen, is that we were prepared for AIDS because, in 1978, we established five interdisciplinary centers for research on immunologic diseases. One was at UCLA [University of California, Los Angeles]; in fact, that was the center that reported the first cases. We could not have been more prepared. These centers, as well as our STD centers, got involved right away when [Dr. Robert] Gallo had the nose to think that the cause was a retrovirus, and that was very perceptive. But we still did not know what the virus was.

I think it was in 1982, Ken Sell could tell you, that we held a meeting at the NIH, on the possible candidates for virus causes. A number of people attended. Albert Sabin chaired. He did a very good job. I do not know whether there is a transcript of that meeting, but Sabin did a very good job of summarizing, including asking the questions of why now, why these people, and so on. That meeting was a very good summary.

One of the things that I have been criticized for is that when we were asked whether we had enough money, I did not immediately ask for a lot more money. I guess this caution was from my early concern about running too fast after a few cases. It does not mean that we were not concerned about those individuals because they were gay. That was not it at all. Our budget requests were written in the context of numerous things that had to be done. This was one more problem with a limited number of patients. Also in my own mind, we were already tooled up. We had a lot of people ready to work, and they could work on AIDS. They already had money from research grants and center grants. Scientists are always going to say they need more money or they cannot do a thing with what they have. But that is not true. In 1968 when the STD epidemic began to heat up, we (at Rockefeller) began working on gonorrhea and used funds to do so at the start from my grant to do research on streptococci. So there is flexibility in the system.

Harden: A number of people have written quite emotionally that the scientific community should have realized the problem AIDS would become, should have spent more money on it, should have done a lot of things. A number of scientists with whom I have talked said that initially they thought of AIDS, like so many other disease phenomena, as an isolated thing, a curiosity that would probably go away.

Krause: Initially we thought that it was an outbreak of something, that the cause would be found and that would be it. For example, this strange outbreak of hyperthyroidism in Iowa—some of these people were desperately ill. These things happen all the time, but I do not agree with the complaint that the scientists did not jump on it

just as soon as they realized that it was a problem. They jumped on it, first of all, because it was a medical problem, and second, because medical scientists cannot be kept away from rare diseases. They will go after a rare disease even if they have to go to New Guinea, let alone into a gay community in San Francisco. If they sniff out that this is going to lead somewhere, they act upon it. But there is a limit as to how much money can be allocated for every rare disease. On the other hand, if individual investigators sense the existence of scientific opportunity, that is up to them. It is not up to a manager in Washington.

I do not agree that we were slow to respond. Dr. Robin Weiss, who is the director of the Cancer Institute in London, made some remarks recently about how quickly scientific progress has been made since the first cases were reported. In 1981, AIDS was first reported, and in 1982, it was detected as a sexually transmitted disease. I do not think people realize how difficult that was, to identify a chronic disease with a long latent period of three to seven years and to show that it was sexually transmitted. It is one thing to show that venereal disease is sexually transmitted with symptoms appearing three or four days after contact. It is quite another matter to show sexual transmission for a disease with a long latent period. That is tough, and the researchers did it in one year.

In 1983 the AIDS virus was reported and in 1984 the isolation of the AIDS virus was confirmed. In 1985 the blood screening test to detect contaminated blood was devised and put into effect, along with the test for screening of the population on a voluntary basis. Prevention programs and information outreach programs were organized. In 1986 the first clinical trials of antiviral drugs were initiated. In 1987 and 1988 a prototype vaccine was already in trial. In 1988 clinical trials were underway to determine if a soluble CD4 receptor would prevent AIDS virus infection of cells. All of that in seven years. That is quite a response, and so I think we did respond very rapidly. Once it was clear that the disease was sexually transmitted, people began to work on it pretty fast.

If you review the work at the STD centers around the country--their annual reports, the reports of the immunologic and allergic centers that we established, and the reports of the centers of the Cancer Institute--you will find that recognition of AIDS as an STD was a big turning point.

I think NIAID needed more research money, not just for research on AIDS but for research on the immune system, on virology, on vaccines, on drugs and more research on the secondary infections. All AIDS patients get secondary infections, but research on some of these was not adequately funded.

Harden: One criticism of NIAID was that in its initial response to Congress, it listed a certain number of grants in basic immunological research as AIDS grants. What

was the rationale for doing this? Did the Institute believe that more needed to be done in those particular areas, or was it really just padding the record?

Krause: I would have to go back and look at the congressional testimony. I think that we took the view, although I would have to go back and look at the notes, that a great deal of research in immunology clearly was relevant to research on AIDS, because early on we thought it was primarily an infection of the immune system. We now know it is more complicated than that. We certainly knew that it resulted in great aberrations of the immune system and therefore we were spending money on such things as the lymphokines, interferon, and the interleukins, etc., which certainly was research that had to be done to understand AIDS. Furthermore, these substances have since been used as candidates for treatments. Some of what we did was research that supported AIDS rather than AIDS research directly.

I do think that we stimulated scientists to move into AIDS research. I suppose, in retrospect, you could say that if we had come out with a program announcement involving megabucks, then people would have stopped whatever they were doing to work only on AIDS. My view is that, in general, if it is an interesting problem then clinical immunologists and virologists will start working on it. They will keep doing what they are doing, for example, working on lupus, but they will also start working on this new problem. Once they need more money, after some preliminary work in research, they will apply for it, and if it is in an important area, they will get it. One of the things we did do, perhaps in 1983, was to decrease the time it took to get the AIDS grants reviewed. If somebody had preliminary observations and wrote a grant application, and the study section approved it, the NIAID Council (secondary review) was polled by mail ballot. Therefore, we did not wait for the next Council meeting to get approval for funding. This decreased the time from application submission to grant award by three months.

Harden: One reason that we are here talking about this is because AIDS has become such a major concern.

Krause: Before we leave the subject, let us get back to another criticism. I went over this in considerable detail with Randy Shilts. He was very critical in his book about something I said. The gay community was upset with us, and the doctors who were taking care of gay patients were upset with us. We were not directing research money to them. I said something to the effect that practicing physicians are not necessarily the people who can best use the research money. That does not mean that there are no practicing physicians who do research. Some do receive research support by the NIH. But, in general, they are not the primary recipients of these research grants. Randy Shilts took that to mean we did not want to fund research by any practicing physician, which I did not mean at all. It happens to be true that the best use of research funds is by people who primarily do research.

Furthermore, I think there was confusion in the gay community about the purpose of NIH funds. They needed money for treatment, for patient management, and for support of the health care delivery system for the AIDS patients. They wanted help, whether it was from the NIH or the Public Health Service. They did not care; they needed help. I understand that. I understand their frustration because we only do research, and the CDC says that they only do surveillance. So who was going to help the gay community? They had sick folks out there. I understand that.

I asked Jack Whitescarver early on to take on the responsibility for outreach. NIAID had never had that mandate. The Cancer Institute ([NCI], the Heart Institute [NHLBI] and the Aging Institute [National Institute on Aging] have outreach activities like social research, behavior modification, and demonstration projects. Even without the legislative mandate from Congress, we started with a series of programs all over the country.

We presented to the afflicted communities or to the health care workers all the information we had on AIDS. I went to one meeting in 1982 at UCLA where I spent an extra day going to a gay treatment center that had been organized for STD and behavioral counseling; for all the social problems that these young men and some women had when they left Midwestern homes to come to California. I met with the board of directors. They were a hostile group. It was a hostile meeting. They really were not interested in whether the NIH or the CDC did research. They had a large number of sick people, and they needed help. As they saw it, all we were giving them was a bureaucratic alphabet soup (CDC, FDA, NIAID, NIC, NCI, HICFA, etc.). I understand that frustration.

We (NIAID) held four or five meetings in various cities on health and prevention matters pertaining to AIDS. I think that all the meetings were useful, not only for those patients who had the disease, but also because these meetings got information out early to a large group of people. We had a meeting in downtown Washington, D.C., at the Hilton, in which the ballroom was completely packed. It was so full, we called Dr. Ed [Edward] Brandt, Assistant Secretary, DHHS, and said that he had better come over and talk to these people, which he did. NIAID took the lead in these outreach activities.

Harden: What has happened to those programs, do you know?

Krause: I do not know. Jack Whitescarver was responsible for them, he got a citation for his work, and so you need to talk to him about that. He will have the early history. That is one of the proactive steps we took.

Then I started working very closely with the President of the Society of Physicians for Human Rights, Dr. Neal Schram, an internist from California. I worked very closely with him early on and with his successor. They developed respect for my

contributions and asked me to be their banquet speaker at the annual meeting in Chicago in 1984. This is primarily a group of gay and lesbian physicians. I can give you a copy of my talk if you would like to read it. The theme is taken from a letter from Anton Chekov to his brother after he had gone to the penal colony in Sakhalin Island and taken care of the prisoners there. The prisoners were outcasts of Czarist Russia. I took the title of the talk from a remark that he had made. "Does the rough garb of the convict hang in your wardrobe? Let it hang there." Chekov wrote to his brother Michael, saying that he was satisfied with what he had done and that he could say with peace of mind that the rough garb of the convict now hung in his wardrobe. He had done something for humanity. I was very pleased because when I finished the talk, I got a standing ovation, the only one I have ever received. I had worked very hard on that talk. It meant a great deal to me that NIAID's efforts were recognized in this way. This was in 1984.

Harden: One of the reasons that we are talking about AIDS is because AIDS is not just any disease, but it is a disease that has evoked an enormous public outcry. Dr. Fauci said that he believes it is the first disease virtually to force scientists to publish in the press rather than to publish in scientific journals. This is where I want to get back to your World War II experience. Could you make some comparisons as to how the public health community looked at sexually transmitted diseases then, how it looks at them now, and how the public reacted to the kinds of things that the medical community did to respond? Are there comparisons?

Krause: Yes, there are. There are very interesting comparisons. I was a young nineteen-year-old boy at the time of World War II, but news about venereal diseases made quite an impression on me. I did not know anything about venereal disease when I went into the army, but within the first three weeks I had learned a lot, not by personal experience but by what they told us. The Army doctor talked to us about venereal disease: syphilis and gonorrhea. We were shown movies in technicolor of syphilitic chancres on penises and vaginas and a gonorrhea-infected penis with the pus coming out of the urethra. We were shown sociological movies about a soldier picking up a prostitute and not having a condom with him. Three days later he is shown coming away from the urinal with fright on his face because he urinated pus.

The doctor showed us how to put on condoms using a broomstick for a dildo. That got a big laugh. "Here's John," he says, holding up a five-foot broomstick, putting a condom on one end of it. He told how to hold the penis just below the glans and to leave about half an inch of condom at the tip so there is room for the ejaculate. I remember the sergeant telling us later, "You guys remember that I slipped one on too tight once and when I came, my God, I thought it would blow my balls off."

In wartime, the language was pretty much as you would imagine. I remember when I was taken in, everything was said in the coarsest language you could imagine--at the dinner table: "Pass the fucking butter, pass the fucking soup, pass the fucking milk, what the fuck, what the fuck are you fuckers thinking about," and so forth. You have to realize it is probably part of the process of depersonalizing people, so that they are better prepared for combat. In any event, it happens, it is probably sad. You get all that if you read Norman Mailer's The Naked and the Dead and other modern war literature, you really get absolute coarseness. There is a certain relationship between coarseness and laxity in sexual morals. Language was coarse and very explicit. In many ways Mailer's novels can not compare to All Quiet on the Western Front and The Red Badge of Courage--no overt coarseness in those.

Now let us go to the control side during World War II. We did things then that would be called infringement of human rights today. For example, everybody had a Wassermann test, and you had no choice. That was also true in the civilian community in those days; a premarital Wassermann test was required. Before penicillin, the infected recruit had to be started on long term syphilis treatment invented by Paul Ehrlich.

We had "short-arm" inspections, which meant inspections of the penis. Often there were spot checks at three o'clock in the morning. The lights would go on in the barracks, and we would hear, "All you fucking bastards get up and put on your shorts and raincoats and nothing else, and go outside, and when the doctor passes in front of you, open the raincoat and show your cocks." Then you were asked to strip down your penis to see if there was any pus in the urethra. We were a bunch of young guys, so some of them may have just had a wet dream, and on some occasions guys would be hauled out. I must confess, I do not know whether gonorrhea was ever detected in this way. I do remember several guys who had to go over to the dispensary, but it was just semen in the urethra and not gonorrhea pus.

We also had green light stations or "pro" [prophylactic] stations, and there was tremendous propaganda urging us to use the stations. Whether it did any good or not before penicillin, I do not know. The treatment was soap suds and thirty milliliters of argerol solution injected up the urethra. It stung like hell. As a medic, I gave many of them. All this changed with penicillin. "Queen penicillin," it was called.

We had case contact reporting, and I did this for several months in venereal disease control work. I took a two-week course in which I was instructed on how to get a soldier to tell you whom he slept with and from whom he got venereal disease. When we learned the woman's name, we reported it to the U.S. Public Health Service authorities so they could find her and treat her.

It took interviewing skill to get that information. You can say that this was extracting information from the soldier by means that might not be acceptable today. A good interviewer could usually get the name. I remember the first time I interviewed a soldier, I did not get the name of the girl. After an hour-long interview, the sergeant who was in charge of this unit in Fort Riley, Kansas, went in and said, "Well, okay, let's see what I can do." He went in and five minutes later he came out with the name. I do not know whether he threatened the soldier, but I bet he did.

When a rated soldier no longer had sergeants' stripes and just a silhouette on his sleeve where the stripes had been, you knew he had probably been busted because he got venereal disease. I suspect cooperating with the interviewer was a way of protecting your rank. Sort of a quid pro quo.

You could be broken back down in the ranks and even officers were broken from officer rank to the non-commissioned ranks. It was our responsibility to use a condom, and not to get venereal disease. Period. If you got venereal disease, it was not in the line of duty.

After penicillin, everything was more relaxed. That is the World War II experience. I think in regard to STDs, we did things in the context of the military. Even the civilian population was treated this way. We griped about it, but after all there is nothing fair about war. It is hell.

Harden: Could you draw some comparisons with how the public health community and the public view the same issues with regard to AIDS, like the use of condoms?

Krause: We have been in a very strange situation. It is probably fair to say that if there is any place where the Public Health Service did less than it might have done, it has been in public health education about AIDS, although Dr. Koop did a great deal. The information needed is about the risk of sexual and blood-to-blood transmission. In World War II, the information on the risks and on behavior modification was handled very explicitly. Now with AIDS, matters have been handled very gingerly. The English have done it much better. It is a paradox, because we have gone through a great sexual revolution and there is greater acceptance of sexually related information by the general public, in both the gay and the heterosexual communities. We are living in a period in which the divorce rate is almost fifty percent and in which there is a good deal of sexual activity out of wedlock. Nevertheless, for reasons that are not entirely clear, there has been a restraint on what the Public Health Service can say publicly. "Chic" [Dr. C. Everett] Koop has gone right ahead, and I admire him for it. He came in as a Surgeon General who was supposed to be an arch conservative, against abortion and, therefore, presumably very safe. Furthermore, though he looked like Moses,

he ended up talking about the use of condoms. I do not think the White House knows what to do with him.

Harden: So you would say that the reason the Public Health Service did not move as rapidly as it might have in education of the public was due to political policy pressures.

Krause: I do not think it is just political. I think political policy represents the public's social outlook. I think that the public, on the one hand, behaves one way, but on the other hand, its nature is conservative. It still values behavior from a stricter past. It behaves one way sexually, but its social outlook is different. I am not really blaming the [Ronald] Reagan administration. I think that Reagan and the people have what they want. They want it both ways. They want to be sexually free and at the same time they want to give the appearance of faith, God, family, and so forth.

In an Anglo-American conference Whitescarver and I organized a year ago in September (1988), the purpose was to identify similarities and differences between the American strategy to combat the AIDS epidemic and that of Britain.

In 1983 or thereabouts, Sir James Gowans, the head of the Medical Research Council (MRC) visited us and by then I was convinced that they (England) had to do something to get ready. I had known Gowan for years; we are the same age, and we both went into government at the same time. I left Rockefeller, a very pristine place, and came to NIAID. He left Oxford, also a pretty pristine place, and went to London as the head of the MRC in 1975. So, in 1982, he said, "What should we do?" and I said "Get ready." He said they did not have any cases there, did I think AIDS would come? I told Jim that it certainly would since it is a sexually transmitted disease and there was no way to keep it out of England. People travel worldwide. In 1983, I said the same thing to Sir Gustav Nossal, Director of the Eliza and Walter Hall Institute [of Medical Research] in Australia. As a result, they did things differently. Many feel that they did not do enough, but they certainly did prepare for the epidemic.

It is impressive what the British have done in the public information arena, under the direction of Dr. Spencer Haggart, chief executive, Health Education Authority for England. He talked about the four objectives of their campaign. First, to educate with the facts, second, to dispel myths, third, to give advice on prevention, and fourth, to provide information on behavior modification. They have had two campaigns to inform the public, one was two years ago and the other was more recently. These were covered by newspapers, television spots, the whole bit, and they had letters from [Prime Minister] Maggie [Margaret] Thatcher. They also put in a program to evaluate their campaign. Their information, as we saw on their television clips, was very explicit, they were not little pansy things. As far as I

know, we have not even got our television clips out yet. It is not the CDC's fault, it is just that the CDC has not been able to come up with something that would not be offensive to the television audience in this country. It is beyond me, what with Dallas and the soaps on television. The British used very explicit material.

Their first questionnaire was designed to see what the general British population felt. Did the people believe that explicit information was offensive? Only five percent thought so. Ninety-five percent thought it was appropriate. Seventy-five percent of the adults had read or at least looked at the information leaflet. After the information program, a survey indicated that among the general population, casual and anal sex was reduced by fifty percent. Among homosexuals, the number of partners per year fell from more than ten to four.

It was clear from the survey that there was a negative attitude toward the use of the condoms, and advertising was needed to constantly reinforce a positive view. The British evaluated again with a second survey, and the phone calls to a hot line doubled. The calls from women went from thirty-three to fifty-four percent, which is interesting from the angle of safe sex, since it means you were doing something. The demand for HIV [human immunodeficiency virus] blood testing rose by 300 percent. Serious press such as the Times of London felt the information campaigns were acceptable, but the tabloids, as one might expect, were hostile.

The Dutch and others have gotten themselves much better organized. Several years ago, the Minister of Health, a woman, when on television, had a dildo, a dummy penis, on which she put a condom to show people how to use it. I can not imagine Mrs. [Margaret] Heckler having done that. We have fallen behind here, but I think the Public Health Service, in general, should be in the lead position. In this instance we may not have provided as much leadership as we should have, but I also think that when it comes to matters of sexuality, the government can not go too far beyond what the people themselves are prepared to accept.

Harden: When you left NIAID in the summer of 1984, the AIDS virus had been identified. You moved from a government position into an academic position at Emory University School of Medicine. What can you report about investigation into AIDS and the reaction to it from outside the government?

Krause: There are various aspects to that. It certainly is true that there was concern in the medical community, particularly among those who were involved with taking care of these patients. They were overwhelmed. They were working very hard in infectious diseases, but internal medicine people were and are the lowest paid of the specialties along with pediatricians. A single AIDS patient on a given day may take as much of an internist's time as the time a surgeon takes to do open-heart surgery.

I do not mean to say that internists were not taking care of the AIDS patients because of this. They were taking care of the AIDS patients. I do not mean to say that they were grumbling, but they were overworked, and they were among the underpaid of the health profession. How do we get more physicians to take care of people in the sub-specialty of infectious diseases? I do not know.

Another area that is a matter of concern relates to the health care workers in intensive care units, during surgery, and so forth, who feel that they should have the right to know if a patient has AIDS, because then they will take different precautions. I can see both sides of this issue. In the days of the tuberculin test, if you knew a patient had tuberculosis, the precautions you took in chest surgery were entirely different than for the non-infected patient. The medical professional was at great risk from tuberculosis. Now people are at risk in taking care of people with AIDS. That does not mean they are not going to do it, but they are at risk. If they have to treat every patient as if he or she is a potential AIDS patient, procedures become difficult to manage. I think this is an ethical issue, and on this I come down on the side of [Dr.] LeRoy Walters, an ethicist. There are those who favor and those who do not favor selective screening. It is Walters's belief that testing is morally justifiable, if it is accompanied by counselling, by protection of confidentiality, and if there are built-in safeguards of non-discrimination for those who are AIDS-antibody positive.

In regard to the subject of health care and the duty of health care workers to give care to everyone, it is Walters's view that if the general measures for infectious disease control in the hospital do not work to prevent the spread of the disease to health care workers, then it would be appropriate to freeze blood for surgery patients and other patients who might be at high risk to personnel. I think sooner or later we are going to have to come to this, but as he said, the safeguards have to be built in.

From several points of view, I developed an appreciation of the frustration and even anger of the gay community concerning their perceptions about the medical response to the AIDS epidemic as a consequence of my experience at Emory University School of Medicine from August 1984 until January 1989. When I went to Emory in 1984, I assumed we would become a major center for AIDS basic and clinical research, patient care, and a center for clinical trials. We had the CDC next door. We supervised Grady Hospital, a large public county facility. Atlanta was known to be a city with a large gay population. But to this day, Emory has no comprehensive AIDS program. So what went wrong? The fact is all of my efforts to develop such a comprehensive program were stonewalled by the Southern establishment of Atlanta that decides such matters. I do not even know who they are. You do not hear from them directly. You do not get told directly do not do this or do not do that. You get word secondhand.

Was it homophobia? I do not know. The Atlanta Constitution wrote an extensive article on the "do nothing" response of Emory. It is a very good article and should be referenced to this interview. Atlanta should have had the most comprehensive AIDS center in the South. Because of our inaction, the University of Alabama, Birmingham, and Duke University have taken the lead. So I now understand the frustration of the gay community concerning their perceptions of a slow response to the challenge of AIDS. I was not prepared for the social attitudes of the deep South. I had lived in New York City for twenty years and in Washington, D.C., for ten years. Issues of life style were not so controversial as in the South. Indeed, in the South, as near as I can tell, controversial issues are better left unsaid. So as I say, I now know full well the frustration of the gay community.

Harden: Do you recall when you first realized that AIDS was occurring internationally--in Africa and other countries, Third World countries and Europe? Could you give me some perspective on this?

Krause: NIAID had a good deal to do with that, and I think the institute has not been given the credit that it deserves. That is behind me now, of course. I have had enough honors and glory, and I do not need to worry about that too much. But it does put the story in perspective. We knew there was a "Haitian connection." Early on we had the four H's--hemophiliacs, homosexuals, Haitians, and heroin addicts. We could not get into Haiti because they were so damned mad that we called AIDS the Haitian disease. It was not a disease of Haitians. It was true that there was an unusual percentage of people of Haitian origin with AIDS living in the United States. That is why we came to use that phrase to identify them. By Haitians we did not mean the people of Haiti.

The Public Health Service could not get into Haiti in 1983, because the Haitians were so angry, but on the other hand, Haitian tourism was falling off. Haiti needed help. [Dr.] Karl Western was a big help here. He is somebody you should talk to. He had worked with PAHO [Pan American Health Organization] before he became my special assistant for international health. He organized a meeting between the assistant minister of health for Haiti and PAHO. PAHO was neutral ground. The Haitians were incredibly angry with us, but we had a good discussion, and they extended an invitation for us to go to Haiti. It was in the spring of 1983. I took Dr. Tom [Thomas] Quinn, an epidemiologist, and Dr. Clifford Lane, a clinical investigator, with me. Also somebody from the CDC [Dr. Harry Haverkos]. I have forgotten his name now, I apologize for that. We got there and were met by the assistant health minister. He took us to the hospital, where we were going to talk with Haitian doctors, but the doctors were so angry with the Americans that they would not talk. The assistant minister said that the Americans were going to see AIDS patients, even if he had to take them on rounds himself. So we did go on rounds, and the first three patients we saw were women, and three or four of the first ten patients had tuberculosis. This was new

for us. A large percentage of women, and tuberculosis as an opportunistic infection.

Once we finally got over the first rough hurdles, we reviewed their data with Dr. [Jean] Pape, a Haitian doctor who had trained at Cornell [University] and who was already working with our STD unit or our tropical medicine unit or both at Cornell.

You know that people think the scientific community did not do anything, but, my God, it is like the free marketplace, all kinds of things go on all the time that go unnoticed. I did not even know this doctor until I met him. He was very well trained, a very good clinician, who had been interested in diarrheal diseases.

We won the local doctors over. Pretty soon they came around to our hotel and talked. We spent ten days there, and at the end it was quite clear that there was a community in which AIDS was being spread. Homosexuality in Haiti was probably a livelihood, not just a way of life. AIDS was going from male prostitutes to females. Now it is history. But we helped out and the young doctors came to the NIAID clinical services to learn more about AIDS from Dr. Fauci.

Haitians are wonderful people. I brought home art, and I enjoyed the people tremendously. They are French-speaking, extremely artistic, and talented people. They have a tragic history, and because of this, large numbers of them in the 1960s had gone to Zaire as engineers, accountants, etc. When they were kicked out, some of them came back to Haiti, some of them came here and to Canada, and a few went to Europe. AIDS travelled with them from Africa.

My own view is that AIDS started in Africa, because of societal changes and urbanization. It had probably been confined and transmitted very sporadically in the rural communities, not spreading very far because people did not travel very far. Since they have a lot of STD, something must have happened to the social barriers, and the diseases broke out. Certainly in recent times prostitution has flourished in the large urbanized cities of central Africa. That is a change.

Since the introduction of Western medicine and the needle, many medicines are given by needle injections. Patients demand needle injections, and as a result needles are used over and over again. Undoubtedly this fostered the spread of AIDS.

Whatever the reasons, all sorts of social changes resulted in an epidemic. Infectious diseases take advantage of what I call undercurrent opportunity. Malaria is a good example. In World War II, malaria was reported in Archangel, north of the Arctic Circle, for the first time in history, but now it has retreated all the way back to the tropics. The mosquito is still there in Archangel, but malaria

is not. There is an old saying in the Mediterranean, that "malaria flees before the plow"; but, as I have noted "it returns on the wings of war." Undercurrents of opportunities—it is true for every infectious disease.

In the summer of 1983 in Vienna at the international conference of infectious diseases, I gave a talk on "Koch's Postulates and the Search for the AIDS Agent." It was published in 1984. Many people have quoted that paper because that is where I suggested that AIDS might have always have been there in Africa, and that epidemiologic changes had brought it out. The paper set forth useful ideas in the epidemiology of AIDS in a historical context.

In Vienna I met Dr. Luc Eyckmans, the head of the Institute for Tropical Medicine in Antwerp. Quinn, Whitescarver, Western, and Peter Piot (Belgium) were there as well. We planned the strategy for getting into Zaire. We set up a program in which the Belgians would be involved. Later Quinn and I went to Antwerp for future planning. We got together a team and about that time we bumped into the CDC doing the same thing. [Dr. Joseph] McCormick and [Dr.] Jonathan Mann, from the CDC, wanted to do their own thing and did not see why NIAID had to get involved. As far as I was concerned, we had to be involved because, by congressional mandate, the CDC can only take research a certain distance. So we ended up with a compromise. Ken Sell can tell you more about that. The compromise was that the CDC representative was the director of the project and the NIH person was the director of the laboratory. Since then, Project SIDA has been a very productive and important laboratory. But get the full story from Quinn, Sell, and Dr. Henry L. Francis. Francis was NIAID's person in Zaire. That is the story of my international connection.

There was one other consequence of the meeting in Vienna (1983). In the talk I gave there, I spoke about the importance of the natural history of infectious diseases. This is a subject that is oftentimes overlooked today. The natural history of a disease is concerned with all aspects of its manifestations, from beginning to end, and the circumstances surrounding its occurrence. Natural history requires the skills of the clinician, the scientist, the epidemiologist.

I recognize that we would need to study many patients for a long time, from beginning to end, if we were to learn about the full complexity of AIDS, the variation in the course of the disease from one patient to the next, etc. In the 1920s and the 1930s, Drs. T. Duckett Jones and Edward F. Bland did the landmark study on the natural history of rheumatic fever and rheumatic heart disease. This disease can have many different permutations and combinations during its course. In some instances, the disease can progress very rapidly, in others, it progresses very slowly. Many patients live a normal life with heart disease, and in others there is a rapid decline. I knew that we would have to do something similar to the work of Jones and Bland for the study of the natural history of AIDS.

So we organized the Multicenter AIDS Cohort Study (MACS). This was a program in which grants were awarded to four or five clinical centers in the United States. It was their job to follow the natural history for as long as it would take to learn about the manifestations of the disease from beginning to end. One important aspect that has emerged from this study is that there are those individuals who seem to do quite well during the course of their infection. In fact, some do remarkably well, and therefore an important area of investigation concerns the reasons some people, although infected with the virus, do not come down with AIDS for a long period of time. What are the immune mechanisms in such people that result in a long delay in the occurrence of AIDS? Much has been learned from the Multicenter AIDS Cohort Study, and you should get more information about it from those in NIAID that are responsible for it. I think the MACS was probably one of the most important contributions that I made to the AIDS epidemic in addition to the initiative that led to Project SIDA in Zaire. After all, had I not done that, perhaps Jonathan Mann would not now be famous.

Harden: Before we stop, is there anything else you would like to say?

Krause: Yes, one thing that I think is important is to draw a parallel with syphilis. [William] McNeill gave a very important commentary on this, in his book Plagues and People. He emphasized that syphilis had little demographic effect because those who died of it would have died anyway from something else. This is not true in the case of AIDS. McNeill traced the influence of syphilis in the context of the emergence of Puritan tradition in the seventeenth century, 100 years after syphilis got going. When syphilis finally settled in, it became a disease of those at the top, the nobility, and those at the bottom. Neither group was "contaminated" by Puritanism. As a result, syphilis was a devastating disease for the lower orders and it also decimated the ruling houses of Europe. The Puritan middle classes prospered. McNeill concludes that the rise of Puritanism grew out of the efforts by the bourgeoisie and the middle class to protect themselves.

I have written recently, and I will send you a copy, about the history of syphilis in this century. From 1900 to 1910, there was a decade of discovery that transformed our understanding of syphilis from ignorance to "magic bullets." The decade started in 1900, after almost thirty years of research. Although many people had tried, no one had been able to discover the cause of syphilis. It was assumed that the cause was an infectious agent, but there was no treatment. In 1903 the organism was found. Before the organism was found an animal model became available. The infection could be maintained in the cornea of the eye of the rabbit and in the testicles of the rabbit. You can transfer the organism from the testicle of one rabbit to that of another rabbit. [Dr. Paul] Ehrlich began his research looking for an arsenical "magic bullet," and the Wassermann test was developed. The Georg Speyer Haus was formed in Frankfurt, and a Japanese chemist joined Ehrlich. If you read Ehrlich's notebooks, he started with compound 306 and ended up with compound 606. He did 300 experiments--most of them failures--and then, of course, with the success of 606, he developed Salvarsan (arsphenamine) as a treatment. The drug cured the experimental infection in the rabbit. In humans with syphilis this drug for the first time caused a reversal of the Wassermann reaction. With treatment, the patient's blood test would go from positive to negative, and this had never been seen before. Prior to the treatment, once you were positive you remained positive.

At first, it was hard to get a pharmaceutical firm to manufacture arsphenamine, but then they could not make enough. There was criticism, terrible criticism, that they were making too much money, that the drug cost too much, and that Ehrlich was profiting from it. He never did profit from it. Some money went to the research at the Speyer Haus in Frankfurt, but he himself did not profit. There was a social reaction, a prediction that with an effective treatment people would become more licentious. In a sense, the story of syphilis provides a parallel for the story of AIDS.

Harden: Thank you, Dr. Krause.

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