This is an oral history interview with Dr. Richard G. Wyatt, Office of the Director, National Institutes of Health (NIH), who formerly occupied a post at the National Institute of Allergy and Infectious Diseases (NIAID). The interview was conducted by Dr. Victoria A. Harden, Director, NIH Historical Office, and Dennis Rodrigues, program analyst, NIH Historical Office, on 28 March 1990.

Rodrigues: Maybe we could start the interview by discussing why individuals choose their line of work. Why did you decide on a career in medicine?

Wyatt: That goes back further than I thought you were going to go. A career in medicine in my case goes back to a high school interest in science fair projects. Initially I made a photoelectric eye in the ninth grade; it won fourth place in the Lebanon High School science fair--that is in Missouri. After that I quickly switched to biology. During my sophomore year, in 1958, I did a project in tissue culture. I took some embryonated eggs, removed the embryos and transferred them over into some tube cultures, and watched them grow to a certain extent. I am not sure how well they grew but that was my early tissue culture work. In 1959, I moved on to histopathology, comparative histopathology of liver tissue, in which

I took livers from various species beginning with crayfish liver, or, at least a digestive organ. We even got a fixed specimen of a human liver from a local area pathologist.

Harden: Did you come from a medical family that encouraged you to do this?

Wyatt: My uncle was a doctor, and that probably did influence me. It was interesting to compare the morphology on these different livers. Also that same year, I remember our high school biology class--this was advanced biology, Biology 2--sent away to the American Type Culture Collection for some Rous sarcoma virus. We injected the Rous sarcoma virus into a series of chickens and followed the tumors that developed. I do not think high school students would be doing that kind of experiment today but that was in an era before things were highly regulated. So we had our chickens with the Rous sarcoma virus tumors and we watched their development. It worked together very nicely with our histology studies; we sectioned them [the tumors] and looked at the histological features. I remember that several years later, after I was here at the NIH, we went to a "Perspectives in Virology" meeting in New York. This was in about 1974. I met Mrs. Rous and that is what

reminded me of those projects.

Rodrigues: Could you now move forward in time and tell us about your professional experiences immediately before you came to the NIH, or perhaps the circumstances surrounding why you came to the NIH.

Wyatt: When I came to the NIH it was during the era when each of us, as a physician, had an obligation to the Federal government in the form of a Selective Service obligation, and I had a choice to make. I was involved in pediatrics and I had a choice between either going into the army to continue my pediatric training or coming to the NIH and doing biomedical research as a research associate. It was a very easy choice to make because, as I mentioned, my interests in doing science went all the way back to high school and had continued during college and medical school. In medical school at Washington University [St. Louis], we had the option of doing research in our senior year. Most of my senior year was committed to doing infectious diseases research with Dr. Ralph Feigen, who has moved on from Washington University to Baylor College of Medicine. He is now chairman of pediatrics there and still very involved in infectious diseases research. Making the decision to come to the NIH, and, specifically, to seek out an

area in infectious diseases research was a very easy one. Initially, I fully intended to go back to Washington University or to another university and continue in academic pediatrics.

Harden: I want to explore this a little more. I have asked a number of people that I have been interviewing was it the interest in science [that kept you in research] or were you not interested in going into private practice? In other words, was it either academic medicine or research as opposed to private practice. I am taking a poll of various people to see what factors influenced that decision.

Wyatt: I tend to shy away from the routine that private practice becomes or would become or I thought might become. That was something [a viewpoint] that I came to without ever having experienced private practice. Since I enjoyed patient contact, however, I had every intention of at least going back into an academic setting that would have placed me squarely in contact with patients. Knowing that I like variety in what I do, biomedical research is a "natural" because it is constantly changing and there is never a routine. There is always something new and exciting going on. That is probably the best quick answer.

Rodrigues: With your background and/or interest in infectious

diseases, I assume that you began your career at NIAID.

Wyatt: Yes.

Rodrigues: Which laboratory did you work in--and whom did you work under initially?

Wyatt: I was with Dr. [Bob] Robert Chanock and Dr. Albert Kapikian, who are both still in the Laboratory of Infectious Diseases. Dr. Chanock is the chief, and Dr. Kapikian is the head of the epidemiology section. That is where I landed in 1971. I was invited to be a research associate in that laboratory. When I came here, I did not know which of three infectious diseases I would be working on. There were three options: respiratory syncytial virus; hepatitis, which at that time was largely hepatitis B work; and a new project that had just started a year or so earlier on infectious diarrheas. There were three of us who came as research associates that year. Dr. David S. Hodes, now at Columbia [University] is in pediatrics. His father was Dr. Horace Hodes, who was a well-known pediatrician and infectious diseases specialist many years ago. And [Dr. Stephen M.] Steve Feinstone, who continued in the Laboratory of Infectious Diseases until recently, when he transferred to the FDA [Food and Drug Administration]

with Dr. Gerald Quinnan. He is still in hepatitis research which is where he started in 1971. I began with the group that was just beginning to look at the etiologies of infectious diarrheas. At that point, we did not have any viruses in hand, so we had to start at the very beginning. We were working with a disease and looking for the etiological agents that were associated with that disease.

Rodrigues: Were there certain areas where this disease was more prevalent than others?

Wyatt: Yes. I guess, in a sense, as a pediatrician it attracted me because pediatric diarrheas are quite prevalent and serious in very young children, and in particular in Third World countries. That was not the initial focus of our research, although it came to be eventually. The international aspect was of interest to me because I had spent two summers as a medical student doing research in Guatemala City, at the Institute of Nutrition of Central America, and in Panama, where I had met somebody who was interested in nutritional diarrheas and weanling diarrhea, as we called it. That was [Dr.] Leonardo Mata who is still active in biomedical research in Costa Rica. He stimulated my interest not only in working in Third World countries, but also in the whole area of

infectious diarrheas and malnutrition. It began to fit together. As it turned out, though, when I arrived in the Laboratory of Infectious Diseases at the NIH, they were tackling the problem, not of infantile diarrhea but of epidemic diarrhea and vomiting, which is largely a disease that affects all age groups. The disease would move through a family or an institution, causing diarrhea and vomiting; sometimes one, sometimes the other, or sometimes both, in about fifty percent of the population. We became involved early on in reproducing that disease in volunteers by administering bacteria-free fecal filtrates. We would study the disease that resulted, but, even more importantly, we had the diarrheal stools from those volunteers that we knew contained the infectious agent. It was presumably a virus because we could passage the disease by making bacteria-free fecal filtrates from the diarrheal stools of ill volunteers and passing it again. It was ultimately by examining those fecal filtrates with the immune electron microscopy that we were able to detect for the first time the Norwalk virus, a twenty-seven nanometer virus-like particle that has been associated with the disease. Those studies were headed by Dr. Kapikian.

Rodrigues: I take it there was not a good animal model for this disease.

Wyatt: No. In fact, there still is not for Norwalk virus. We could infect chimpanzees, but without disease.

Rodrigues: Just like AIDS.

Wyatt: That is right. At any rate, animal models for that disease were not there. Later on, we became involved in early studies in rotavirus diarrhea. This got us back into the pediatric age group specifically, because it turns out that the rotaviruses are the most important cause of diarrhea in infants and young children under the age of two. It is a particularly important disease in Third World countries.

Harden: Rotaviruses were what you had been publishing on?

Wyatt: Yes.

Harden: Were you still working on them when AIDS appeared?

Wyatt: Yes. In fact, at the time AIDS emerged there were features about our laboratory that would have made it an ideal laboratory to begin to delve into the etiology of AIDS. I have thought about why we did not do that. It was not a direction that the leaders of the laboratory moved us in. A part of that had to do with the fact that we were making very good progress in rotaviruses and at the time we were developing potential vaccine strains. We had a lot

of work going on in the laboratory dealing directly with preparations that might ultimately find their way into human subjects as candidate vaccines and ultimately as a vaccine that might be used worldwide to prevent rotavirus diarrhea. Of course, when AIDS first came along, there was no way of knowing what the [etiological] agent was. We all suspected it was a virus, but we can talk about that some more. To bring materials, possibly containing unknown etiological agents, into a laboratory where we were working on candidate virus vaccines, did not make sense. Without setting up a totally separate area, it would have been extremely difficult to do that work in the laboratory, so my own "hands-on" experience with AIDS research is rather limited. I recall once doing some studies with Dr. Robert [H.] Purcell, who worked on the second floor of Building 7; I was on the first. We had one room set aside to do some limited studies with materials from AIDS patients. We were particularly interested in growing some cultures for fluorescence staining. We did not actually grow the cultures; we just processed them. The product came, I believe, from Dr. Thomas Folks, who was, if I remember correctly, working with Dr. Kenneth Sell, over in Building 10. He was looking

for any evidence of an infectious agent at the time. We were considering a couple of different possibilities, neither of which turned out to be the agent.

Rodrigues: Some of the people we have talked to--this may be somewhat of a digression--have mentioned that people working in the infectious disease area felt somewhat disenfranchised. There seemed to be so much emphasis on the chronic diseases, and the general level of support and concern expressed by the Congress and the public did not seem to be as great concerning infectious diseases. But there were a number of people who maintained that this was a poor philosophy. How did you view the growth of support for [research on] the chronic diseases and did you feel that it posed problems for those of you working in infectious diseases areas?

Wyatt: One brings one's own perspective to that question. I was, for my first twelve and one-half years at the NIH, working in Building 7 in a laboratory that had for many years been focusing on acute infectious disease processes, whether it was influenza or some of the other respiratory viruses, hepatitis, the infectious diarrheas, etc. In my world we had an emphasis on the acute infectious diseases. I was not

aware of that until, for example, I saw it reflected in the program at the American Epidemiological Society. Both Drs. Chanock and Kapikian were members, and I was invited to become a member in about 1982 or 1983. We discussed that [point] because the relatively small society had focused on acute infectious diseases or infectious diseases in general only a few years before, and it was, at that time, developing a chronic disease orientation. But, specifically, in my own research activity that had not affected us because we were a laboratory involved with acute disease.

Harden: I would like to try to reconstruct the situation when AIDS first appeared. Can you recall when you first heard about the unusual cases, what kinds of conversations went on, and the way thinking developed?

Wyatt: I remember specifically the first time I heard about AIDS. I was in the office over in Building 7, and Dr. Harold [A.] Greenberg, who is now at Stanford [University] and who was in the laboratory for several years--he left about six years ago for Stanford--came walking in with a newspaper article about AIDS that had just appeared. He said, "This is really going to be something important." I looked at

the article and I guess I was not as imaginative, or creative, or perceptive as he was. I said, "You really think so?" I did not see it. This was very early on when the first cases were being reported in the newspapers. So I did not quite capture as he had the importance of it just from reading that initial news report. I do not recall at the very outset the extent of agreement as to the importance of AIDS.

Harden: Had not epidemics occurred from time to time here and there; they came and they went. I think it would be hard to....

Wyatt: Right, but it [AIDS] was not like the other epidemics. One might think about--what is a good example--a dengue-like outbreak or something like that that might occur in a particular part of the world, [or] various arbovirus outbreaks. AIDS was not so circumscribed; it was not so definable. And of course, there was no agent associated with it. It did not have the characteristics, for example, of Legionnaire's disease. That had the characteristics of an acute infectious disease that we were accustomed to, or might think about as [we were] working in the area of infectious diseases. At any rate, it did not take very long, though, before it to begin to sink in that AIDS was going to be important.

Rodrigues: But it is difficult to reconstruct the way people were thinking then because with all we know now we can look back and things seem to be very clear. But at the time, as a number of people have said, when you were actually living with the problem, it was very confusing. Certainly there were no easy answers.

Wyatt: That is right. There were no easy answers. I was just looking back in my files knowing you were coming, and I found an article that appeared, let us see, it was 17 March 1983, in the Washington Post. It was actually the conclusion of a series they did called "New Death--Disease of the Immune System Becoming a U.S. Epidemic." That was March--at about the same time that we did a workshop that we can talk about some more. There were about 1300 cases at that time. Some of the people who were involved then are still very much involved today. It was just coming out--the cases in hemophiliacs were being very clearly recognized. Some of the same people are being quoted; here is [Dr. Anthony S.] Tony Fauci being quoted in this particular news report. You are welcome to have this, if you will give me a copy back.

Harden: That is marvelous. Thank you.

Wyatt: There may be more [articles] before that but that was the one that I happened to keep.

Rodrigues: I was looking through an interview that Vicky had done with Dr. Kenneth Sell, let me pass it to you. He is talking about NIAID's decision as to how they were going to proceed so far as looking at different possible causes. He mentions the work that you were doing.

Wyatt: He did ask me to come over and help. I was still in the Laboratory of Infectious Diseases, but some time between early in 1983 and the following year, I was a sort of special assistant to the scientific director of NIAID on AIDS-related research. It was never actually that formal, but the activity--while there was some laboratory research, albeit very little--initially involved organizing a workshop to consider the various possible etiological agents of AIDS. It was interesting to go back over the workshop in preparation for talking to you, because I happened to save a file on it. It was quite clear just looking through the program that, while we thought the agent was probably a virus, we were not leaving any stones unturned at that point. You can almost tell the direction [of our thinking] based on the way the program [of the workshop] unfolded. We considered a

variety of viruses to begin with, including cytomegalovirus, and I think Dr. Gerald Quinnan advocated cytomegalovirus as the etiologic agent.

Harden: Were there actually advocates promoting other agents?

Wyatt: Oh yes. I do not recall that there was an advocate for the Epstein Barr virus. We certainly talked about it; we talked about herpes virus; adenovirus; the hepatitis viruses, in part because with hepatitis B, the routes of spread seemed to be quite similar. We did have a talk on retroviruses, although I did not see that in the first draft of the program. I found it in a subsequent draft where it was clearly introduced and Dr. Robert Gallo was there to present it. This was a typical NIH workshop, and we were leaving plenty of time for questions. We began to lag behind schedule and Dr. Gallo had to leave. Dr. Edward Gelmann was the scientist working in his laboratory at the time, and actually made the formal presentation. I do not have detailed notes on his presentation but my recollection was that he was talking largely about HTLV-I [Human T-cell Leukemia Virus type-One] at the time and the similarities that they were drawing there with AIDS. There may be a recording of this still around. I think the session was actually recorded, which would be of interest. I

know there was also a recording made of a summary that [Dr.] Albert Sabin did. You may have seen that. It is very rough and it has never been edited. I have a crude transcript of it. So, we did talk about that and we went into a fair amount of discussion on parvoviruses which seemed to have some interesting features that made us think that there might be a clue there. We were talking about some methods for detecting viruses. We talked specifically about immune electron microscopy that we had been working on. Dr. Kapikian gave a nice talk on that using the analogy of how one goes about trying to find a virus or the agent that--using the materials from the disease--reoviruses, even arboviruses. Dr. [Philip] Phil Russell came and talked about possible arboviruses that might be implicated. At one point we had thought we might even get into discussing various kinds of bacteria and parasites that could somehow be involved. That sort of fell away. I guess we realized we could not be so inclusive, and we limited most of our discussion specifically to these various virus groups. But we had a variety of experts--Dr. Clarence (Joe) Gibbs was there to talk about slow viruses, Dr. Maurice Greene, from St. Louis, to talk about papilloma viruses. We really

covered the waterfront and, in fact, in Dr. Sabin's summary, one of his conclusions was that to find the agent, "We must cast a wide net." At that stage in the search for the AIDS agent, we were not at the point where we could focus as much as we might have liked. The other thing that I remember was that Dr. Anthony Fauci had talked specifically about T-4 cells. That had intrigued Dr. Sabin, and he was urging the search to focus on the T-4 cells. This was early April 1983.

Harden: May I ask you about a few more procedural items? You set up the workshop for people from across the country who were interested in AIDS--this came out of NIAID--out of the intramural director's office as opposed to anywhere else.

Wyatt: There were participants from the Cancer Institute. Ed Gelmann was a participant, and Dick [Dr. Richard] Adamson actually talked on the second day, about grant support for studies to search for the AIDS agent.

Harden: Was there any input or initiative from the Public Health Service or the Department [of Health and Human Services]? We are trying to pin down the various sources from which initiatives were coming.

Wyatt: They were certainly a part of the program, because I

remember meeting with Dr. James Curran [from the Centers for Disease Control] on occasion in Ken Sell's office. Curran gave one of the opening talks--an epidemiological overview of AIDS. As best I can recall, this particular workshop was something that Ken Sell wanted to do. So he was talking to Jim and others at the time and Tony Fauci was then a laboratory chief within the intramural program and also had studies that he was interested in.

Rodrigues: Another item that I came across was a list of some of the different projects that NIAID was pursuing. Some of these became well known; for instance, the work that Tony [Fauci] and [Dr. Clifford] Cliff Lane did so far as attempting to reconstitute [the immune systems of] some of the AIDS patients by transplanting cells from an identical twin. But many of these other efforts listed were not pursued. Were these ever published? Or did negative results of this type never get into the literature?

Wyatt: Most negative results do not get into the literature. I think the list probably reflects the interests of Ken Sell. He wanted the intramural program to think about various ways that we could approach the problem. They were ideas that we wanted to try to develop. One of the problems was simply adequate

facilities in which to conduct the different projects. I mentioned earlier that the rotavirus study was a major effort that was ongoing at the time, and now, seven years later, it is still going strong. We are much closer to a vaccine and, in fact, candidate vaccines exist and are being tested. It becomes a management decision on whether to divert attention from another major project. In terms of the rotavirus study, if you look at the impact of rotavirus on infantile mortality, it is extreme. It is a major infectious diseases problem. Ken wanted to try to tap into the expertise that was there and have people think about what they could do, using their skills and the techniques available in their laboratories to look for the agent [of AIDS]. Not long after that, the HTLV-III/LAV [Lymphadenopathy-Associated Virus] story came about, so, quite naturally, many of these things did not come to fruition.

Harden: When did NIAID begin publishing the AIDS Memorandum?

Wyatt: I know it was Ruth Guyer's work.

Harden: She and I were sharing an office and she was in the middle of it [working on the AIDS Memorandum] when I arrived at NIH.

Wyatt: Ruth helped out with this same workshop and, in fact,

we each drafted a summary of the workshop from our own perspective. So she was involved right at the same time. It was probably some time in 1983, but I would have to go back and look.

Harden: Was this another intramural idea to try to disseminate information more rapidly and was it based on the Hepatitis Memorandum too?

Wyatt: That is right. Ruth was working for Ken [Sell] at that time. The idea was to disseminate information as quickly as possible, including those negative studies that you mentioned that do not find their way into the literature. It did not make sense for multiple groups to go out and repeat the others' errors. I do not know how long it continued, but that was the beginning.

Rodrigues: There was one other study that I thought was interesting, at least from its title. You were looking at macrophage cultures for potential AIDS agents. Given the fact that the macrophage is now considered a reservoir of the virus, you may have been looking at the right thing.

Wyatt: I remember an interesting story about those cultures. Tom Folks was doing them up on the eleventh floor in the ACRF [Ambulatory Care Research Facility]. He detected a fungus growing in the culture. Ken may

have told you about this. There was a thought that maybe this particular fungus was producing a cyclosporin-like compound that might have played [a role] in the etiology of AIDS. There was a letter published on it, not a full article, and nothing much happened after that. But it was a product of doing the macrophage cultures.

Harden: When did you get into the project of testing all the different kinds of things that you did?

Wyatt: I do not think we really tested all kinds of things. One of the ways I got involved in the AIDS work was as a result of the idea that we should have multiple samples to test. I became project officer on a contract with the New York Blood Center, and we spent most of our time simply designing a system to try to get the right samples, because we did not know what we were looking for. We knew we wanted to have white cells; we wanted to have populations of T-4 cells to study at some point in the future, and we wanted to have them appropriately stored away. We also wanted to collect them from a spectrum of subjects who were being followed and were recruited by the New York Blood Center, so that when we had the right tests, we could go back and look at them [the samples]. That meant getting the cells frozen away in liquid

nitrogen and getting the various other specimens that we stored appropriately catalogued, making sure that we had the a good data collection system. I was not project officer for too long because I moved to the Office of Intramural Affairs, and Dr. Lois Salzman took over for a period of time. I cannot say exactly how valuable those samples were, because LAV and HTLV-III came up shortly thereafter. But that would have been a valuable repository of specimens from the point of view of studying the natural history [of the disease], because we had earlier specimens from people who subsequently came down with AIDS. Also, the New York Blood Center had specimens already collected from many of the subjects before AIDS was diagnosed, so it was a contract that was set up specifically with the idea of looking at the natural history [of the disease]. The effort expanded rapidly into universities and medical centers around the country.

Harden: What happened to those specimens? Are they still there?

Wyatt: As far as I know, they are still in the freezers. We had a routine set-up for sending them to Bethesda and for storing them away, but I do not know how many of them have been used or studied. There was an

elaborate scheme set up to do the collections.

Rodrigues: After you came over to the Office of the Director [OD] did you have any continuing involvement with AIDS?

Wyatt: I got pulled into it at a time when [Dr. Robert] Bob Gordon was the person designated to attend the PHS AIDS Executive Committee. Bob fell sick and was not able to go, and [Dr.] George Galasso was also pulled in. There were times when he could not go [to the committee meetings], so I found myself during a period of time in late 1984 or early 1985, going to the Humphrey Building to attend the PHS-AIDS [Public Health Service] Executive Committee meetings and reporting on some of the activities that were going on. I was never extremely involved in that. Not too long after that Tony [Fauci] began to play a much more prominent administrative role.

Harden: Was the Office of the Director [OD] involved in AIDS activities at the time of this 1983 workshop or did that come after that?

Wyatt: I am not sure. Bob Gordon's name did not come up in planning this workshop. [Dr. Richard] Dick Krause from NIAID was there and was very much involved; the CDC representatives were there; and the FDA was there. Dick Adamson represented the National Cancer

Institute, but in looking over this particular program, I do not see the OD specifically involved. The first I became aware of OD involvement was when I was going to the OD staff meetings and Bob Gordon would come back and report on meetings that had occurred at the Humphrey Building. I think it picked up speed from that point. Initially, [Dr. Edward] Ed Brandt was still there [as secretary] and very much a part of the activity. When Dr. [James] Mason came in as acting assistant secretary for health, he took a very active role in chairing those meetings. I might have some notes from some of those meetings, although you probably have extensive files from the Executive Secretariat.

Harden: Don't count on that.

Wyatt: I used to come back and write up notes for Dr. [James] Wyngaarden from those meetings so he could see specifically what was going on. Then we would have an NIH meeting, soon after that. Again, this was late 1984 or early 1985, when the representatives from the different institutes would gather in his office to be brought up-to-date on the latest findings.

Harden: Any materials like that that you have I suspect we are going to look at and maybe copy. What do you

think, Dennis?

Rodrigues: Yes. We have been able to uncover quite a few files but one of the things that we have discovered is that some of the people like Bob [Gordon], transmitted a certain amount of their files to OD files. But there were many things that he put down on paper that did not necessarily get filed away. So as far as Bob's papers go, we have not been able to find them all. Much of that material seems to be gone.

Wyatt: Sure. All of this antedates the NIH AIDS Executive Committee that was established later. That came about shortly thereafter and then it all became much more highly organized, with an associate director for AIDS Research and the AIDS Executive Committee at the NIH. There were regular meetings, but I did not get involved in that.

Harden: We are concentrating, at the moment, on the pre-HIV discovery period because it is manageable and it is most interesting how a new disease is discovered. When the formal structures get established, that period is already over. This is why what you are telling us is so helpful and interesting.

Wyatt: There are some interesting anecdotes. I was recalling one time that Ken Sell called us in. He was very excited; he had been hearing about an

organism called Ehrlichia canis. Dr. Charles Kallick had been working on it at Cook County Hospital in Chicago. There were others involved as well. E. canis caused a kind of immune suppression in dogs, and Ken was excited that maybe this was an analogue of the agent that we were looking for in humans. A small group of us went to Chicago one day to talk to these people. Dr. Harlan Caldwell was brought in from the NIAID Rocky Mountain laboratories, because of his expertise on Chlamydia. It obviously did not turn out to be that agent, but we were, to use Dr. Sabin's words, "casting a wide net," trying not to overlook any leads. I think that was another reason for the early interest in the parvoviruses, like canine parvovirus for example. There is a disease [of dogs] that did not [previously] exist and then very rapidly became a major devastating disease of dogs. A vaccine was rapidly prepared to deal with it. But, it is an example of a situation where no disease existed and then, over a short period of time, a major life-threatening disease emerged. Also, take the example of the minute virus of mice. There was a mutation that caused the virus to go from [being] a non-pathogenic virus to a pathogenic virus. So, there were many things to look at for leads, and I

guess that is one of the reasons we had five different talks on paroviruses at this workshop. When we organized it, we simply did not know what was causing AIDS. We even thought about including parasites, bacteria, and fungi on the program, but then we realized that we simply could not do that and limited it more to the viruses.

Harden: So the emphasis by the time of this workshop was clearly on a viral agent as opposed to amyl nitrites or some of the other possible causative agent theories?

Wyatt: Amyl nitrites were discussed. I can see that by just looking through the summary that I prepared seven years ago. It is not edited but we talked about—see here, "Other factors might also play a role; however, it is susceptibility to such an agent (a putative AIDS agent) including an immature immune system, immunosuppression by sperm, immunosuppression by other infectious agents, such as malaria, hepatitis virus or CMV, or `antigen overload'"--whatever that meant at the time. We were clearly looking not only for agents but also for co-factors that might be involved. "The CDC investigators were looking for serologic evidence of infection with known agents." This was the talk that was given. "It was non-

revealing," it says here. Although there was an increase in antibody to hepatitis A and to Treponema pallidum; they were significantly higher in AIDS cases than in controls. They also talked about the studies at that meeting in which they had been trying to isolate potential agents.

Rodrigues: Yes. I think in the interview that Ken [Sell] provided, he talked about how amyl nitrite, which affects vascular permeability, could perhaps render a non-pathogenic agent, given a different situation, allow for a different pathogenic pathway. I could see why it was a viable theory to keep alive until there was something better.

Wyatt: It is an interesting chapter. And it was not that many years ago--when you stop and think about it. Much has happened since.

Harden: We thank you. We may come back and we would like to copy your documents.