

This is an interview with Dr. Richard G. Wyatt, Office of Intramural Research, Office of the Director, National Institutes of Health (NIH), who was formerly a Senior Investigator at the National Institute of Allergy and Infectious Diseases (NIAID). The interview is being conducted by Dennis Rodrigues, Program Analyst, and Victoria Harden, Director of the NIH Historical Office, on March 28, 1990.

Rodrigues: Maybe we could start with 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 [Missouri] High School science fair. 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'm not really 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, where 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 out of a medical family that encouraged you to do this?

Wyatt: My uncle was a doctor, and he probably did influence me. It was interesting to compare the morphology on these different livers and also that same year, I remember that in our high school biology class—this was advanced biology, Biology 2—we 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 don't think high school students would be doing that kind of experiment today, but that was in an era before things were highly regulated. It worked together very nicely with our histology studies; we sectioned them 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—in about 1972. I met Mrs. Peyton Rous and was reminded of that project.

Rodrigues: Maybe you could move up in time, then, and tell us about your professional experiences immediately before you came to NIH, or perhaps why you came to NIH and the circumstances surrounding that.

Wyatt: When I came to NIH it was during the era when each of us, as a physician, had

an obligation to the Federal government, that was the so-called “Doctors’ Draft,” and I had a choice to make. I was involved in pediatrics and I could go to the Army to continue my pediatric training or come to the NIH and do biomedical research as an NIH research associate in the U.S. Public Health Service Commissioned Corps. It was an easy choice to make because, as I mentioned, my interests in doing research went all the way back to high school and continued during college and medical school. In medical school at Washington University, we had the option of doing research in our senior year. I committed most of my senior year to conducting infectious diseases research with Dr. Ralph Feigen, who has moved on from Washington U. to Baylor College of Medicine. He's 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 U. or to another university and continue in academic pediatrics.

Harden: I want to explore this a little more. I've been asking a number of people that I've been interviewing, was it just the interest in science 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'm just 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 that I came to without ever having experienced it. Since I enjoyed patient contact, however, I had every intention of going back at least 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's constantly changing and there's never really a routine. There's always something new and exciting going on. That's probably the best quick answer.

Rodrigues: With your background and/or interest in infectious diseases, I assume that you then began your career at NIAID.

Wyatt: Yes.

Rodrigues: Which lab did you work in—and whom did you work under initially?

Wyatt: I was with Dr. 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's where I landed in 1971. I was invited to be a research associate in that lab. When I came here, I didn't really know which of the three infectious diseases I'd be working on.

There were three options: respiratory syncytial virus; hepatitis, at that time largely hepatitis B work; and a new project that had just started a year or so before on infectious diarrheas. There were three of us as research associates who came that year. Dr. David Hodes, now at Columbia [University] is in pediatrics. His father was Dr. Horace Hodes, as a well-know pediatrician and infectious diseases specialist many years ago. And Dr. 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's 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 really didn't 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 other areas?

Wyatt: Well, yes. I guess, in a sense, as a pediatrician it attracted me because pediatric diarrheas are quite prevalent and serious in the very young children, and in the Third World countries in particular. That wasn't our initial focus of research, although it came to that eventually. The international aspect was of interest to me because I had spent two summers as a medical student with NIH support doing research in Guatemala City, at the Institute of Nutrition of Central America and Panama. There I met somebody who was interested in nutritional diarrheas and weaning diarrhea, as it was called. That was Dr. Leonardo Mata, who is still active in biomedical research in Costa Rica. He stimulated my interest not only in working in the 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 NIH, they were tackling the problem not of infantile diarrhea but of epidemic diarrhea and vomiting, which is a disease that affects all age groups. This disease moves through a family or an institution, causing diarrhea and vomiting: sometimes one, sometimes the other or sometimes both, in about 50 percent of the population. We became involved early on in reproducing that disease in volunteers by administering bacteria-free fecal filtrates. We would observe the disease that resulted, but even more importantly, we then had the diarrheal stools from those volunteers that we knew contained the infectious agent, presumably a virus, because we could passage the disease by making bacteria-free fecal filtrates from the diarrheal stools of ill volunteers and passing the disease again. It was ultimately by examining at those fecal filtrates with the immune electron microscopy that we were able to detect for the first time the Norwalk virus, a 27-nanometer virus-like particle that has been associated with the disease. Those studies were led by Dr. Kapikian.

Rodrigues: So, I take it there wasn't a good animal model for this disease.

Wyatt: No. In fact, there still isn't for Norwalk virus. We could infect chimpanzees, but without disease.

Rodrigues: Just like AIDS.

Wyatt: That's right. At any rate, animal models for that disease weren't there. Later on, we became involved in early studies in rotavirus diarrhea, which brought us into the pediatric age group specifically. It turns out that the rotaviruses are the most important cause of diarrhea in infants and young children under the age of two. It's a particularly important disease in Third World countries.

Harden: Rotaviruses are what you've been publishing on.

Wyatt: Yes.

Harden: Were you still working on it when AIDS popped up?

Wyatt: Yes. In fact, at the time AIDS emerged there would have been features about our lab that would have made it an ideal laboratory to begin to delve into the etiology of AIDS. I've often thought about why we didn't do that, but it wasn't a direction in which the leaders of the laboratory moved us. 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 lab 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 wasn't any way of knowing what the agent was. We all suspected it was a virus, but we can talk about that some more. So to bring materials, possibly containing unknown etiological agents, into a laboratory where we were working on candidate virus vaccines didn't really 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 Purcell, who worked on the second floor of Building 7; I worked on the first floor. We set aside one room in the Purcell lab to do some limited studies with materials from AIDS patients. We were particularly interested in growing some cultures for fluorescence staining. We didn't actually grow the cultures; we just processed them. The product came, I

believe, from Dr. Tom [Thomas] Folks, who worked with Dr. Kenneth Sell 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've talked to—this may be somewhat of a digression—had 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 didn't seem to be as great concerning infectious diseases. But there were a number of people that maintained that this was a poor philosophy. How did you view the growth of support for 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 the first 12 1/2 years here at the NIH, working in Building 7 in a lab 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 wasn't aware of that until, for example, I saw the emphasis on chronic diseases 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 1982. We discussed that because this relatively small society had focused on acute infectious diseases or infectious diseases in general only a few years before; the society had begun to develop a strong chronic disease orientation. But in my own research, this emphasis on chronic diseases didn't affect us because of our long-term commitment to acute infectious diseases.

Harden: I'd like to try to reconstruct the ignorance when AIDS first popped up. Can you recall when you first heard about the unusual cases, the kinds of conversations that went on, and the way the thinking went?

Wyatt: I remember specifically, the first time I heard about AIDS, I was in our office over in Building 7, and Dr. Harry [Harold] Greenberg, who later moved to Stanford, and who was in the lab for several years, came walking in with a newspaper article that had just appeared about what would later be known as AIDS. He said, "You know, this is really going to be something important." I looked at the article, and I guess I wasn't as imaginative or creative or perceptive as he was. I said, "You really think so?" I didn't see that. It was very early on when the first cases were being reported in the newspapers, and so I didn't quite capture the importance of it as he had just from reading that initial news report. I don't recall at the very outset the extent of agreement as

to the importance of this new disease complex.

Harden: Hadn't things popped up from time to time here and there; they kind of came and they went and—I think it would be hard to...

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

Rodrigues: But, it is difficult to reconstruct the way people were thinking back 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 said, when you were actually living with problem, it was very confusing. Certainly there were no easy answers.

Wyatt: That's right. There really weren't easy answers. I was just looking back in my files knowing you were coming, and I found an article that appeared in—let's see, it was March 17, 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—that was about the same time that we did a workshop that we can talk about some more. There were about 1,300 cases at that time. Some of the people who were involved at that time are still very much involved today. It was just coming—the cases in hemophiliacs were being very clearly recognized. Some of the same people are being quoted; here'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's marvelous. Thank you.

Wyatt: There were certainly more behind that, but that was the one that I happened to keep.

Rodrigues: I was looking through an interview that Vicky had taken with Dr. Sell, let me pass it to you. He's talking about their decision—NIAID's decision—as to how they were going to proceed as 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 between sometime early in 1983 and the following year, I was sort of a special assistant to the scientific director of NIAID on AIDS-related research. It was never actually that formal an arrangement, but the activity—while I did some laboratory research on AIDS, 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, although we thought the agent was probably a virus, we really weren't leaving any stones unturned at that point. You can almost tell the direction based on the way the program 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: So, there were actually advocates promoting things as opposed to...

Wyatt: Oh yes. I don't recall 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 didn't 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 lab at the time, and he actually made the formal presentation. I don't have detailed notes on his presentation but my recollection was that he was talking largely about HTLV-I [human T-cell leukemia virus 1] 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's very rough and it's never been edited. I have a crude transcript of it. We had 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 also talked about some methods for detecting viruses. We talked specifically about immune electron microscopy [IEM] that we'd been working on LID [Laboratory of Infectious Diseases]. Dr. Kapikian gave a nice talk on IEM using the analogy of how one goes about trying to find a virus or the agent using the materials from the disease. Dr. Phil Russell talked about possible arboviruses that might be implicated. At one point, we thought we might even discuss various kinds of bacteria and parasites that could somehow be involved. That sort of fell away. I guess we realized we couldn't be so inclusive, and we limited most of our discussion specifically in 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 University, 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 weren't to the point where we could really focus as much as we might have liked. The other thing that I remember specifically was that Dr. Anthony Fauci had talked about T4 cells specifically, that had intrigued Dr. Sabin, and he was urging the search to focus on the T4 cells. This was early April 1983.

Harden: May I ask you a few more procedural things? 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 any where else, and...

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: What, was there any input or initiative from the Public Health Service or the Department? We're just trying to kind of pin down various sources from which initiatives were coming.

Wyatt: They were certainly a part of the program, because I remember meeting with Dr. James Curran on occasion in Ken Sell's office. He 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 Curran and others at the time. Tony Fauci was at that time a lab chief within the NIAID intramural program, and he also had studies that he was interested in.

Rodrigues: Another thing 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 Cliff Lane did as far as attempting to reconstitute some of the patients by transplanting cells from an identical twin. But, many of these other efforts were not pursued. Were these ever published? Or did negative results of this type never get into the literature?

Wyatt: Most negative results don't get into the literature. I think the list probably reflects the interests of Ken Sell. He really 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 the rotavirus study, which was a major effort that was ongoing at the time, and now, seven years later, it's still going strong. We're 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 that is also a public health problem. In terms of the rotavirus study, if you look at the impact of rotavirus on infantile mortality, it's extreme. It's a very 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 using the techniques available in their laboratories to look for the agent. It wasn't long after that, the HTLV-III/LAV [lymphadenopathy-associated virus] story came about, so, quite naturally, a lot of these ideas were not pursued.

Harden: When did NIAID begin publishing the *AIDS Memorandum*?

Wyatt: I'm not sure, but I know it was Ruth Guyer's work.

Harden: We were sharing an office and she was in the middle of it when I arrived.

Wyatt: Ruth helped out with this same workshop and, in fact, we each drafted a summary of the workshop from our individual perspectives. She was involved right at the same time. It probably was some time in 1983, but I'd 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's right. Ruth was working for Ken at that time. The idea was to disseminate information as quickly as possible, including those negative studies that you mentioned that don't find their way into the literature. It didn't make sense for multiple groups to go out and repeat the others' errors. I don't know how long it continued, but that was the beginning.

Rodrigues: There was one other study that I thought was interesting, at least by the title of it. 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 11th 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 be playing 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 kinds of different things that you did?

Wyatt: I don't 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 didn't know what we were looking for. We knew we wanted to have white cells; we wanted to have populations of T4 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. 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 wasn't project officer for too long because I moved to the Office of Intramural Affairs in the Office of the NIH Director, and Dr. Lois Salzman took over for a period of time. I can't 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 AIDS, because we had earlier specimens from people who subsequently came down with AIDS. Also, the New York Blood Center had specimens already collected on 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. 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're still in the freezers. We had a routine set-up for sending them to Bethesda and for storing them away, but I don't 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 OD [Office of the Director, NIH], 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 [Public Health Service] AIDS Executive Committee. Bob became ill and wasn't able to go, and Dr. George Galasso was also recruited as a substitute. There were times when he couldn't go, 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 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 OD involved in AIDS activities at the time of this workshop or was this coming after that?

Wyatt: I'm not sure. Bob Gordon's name didn't come up in planning this workshop. Dick Krause from NIAID was there and was very much involved; the CDC [Centers for Disease Control and Prevention] representatives were there; and FDA [Food and Drug Administration] was there. [Dr. Richard] Dick Adamson represented the National Cancer Institute, but in looking over this particular program, I don't 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, I guess, Dr. Ed Brandt was still there at the time 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. Wyngaarden from those meetings so he could see specifically what was going on. Then we would have an NIH follow-up 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: Anything like that I suspect we're going to look at it and maybe copy. What do you think?

Rodrigues: Yes. We've been able to uncover quite a few files, but one of the things that we've discovered is that some of the people like Bob Gordon transmitted a certain number of their files to OD files. OD files picked up a certain number of files, but there were a lot of things that he put down on paper that didn't necessarily get filed away. So as far as Bob's papers go, we haven't been able

to find them all. A lot 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 didn't get involved in those.

Harden: We're concentrating, at the moment on the pre-HIV period because it's manageable at this point and it's most interesting how one discovers a new disease. When the formal structures get established, you are already through that period. This is why what you're 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'd been hearing about an organism called *Ehrlichia canis*. Dr. Charles Kallick had been working on it at Cook County Hospital in Chicago, and 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 Labs, because of his expertise on *Chlamydia*. It obviously didn't turn out to be the AIDS agent, but we were really, to use Dr. Sabin's words, "casting a wide net", trying to not overlook any leads. I think that was another reason for the early interest in the parvoviruses, like canine parvovirus, for example. There's a disease that didn't exist, and then very rapidly it became a major devastating disease of dogs, for which a vaccine was rapidly prepared to deal with it. But, it's an example of a disease 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 a non-pathogenic virus to a pathogenic virus. So, there were a lot of possible leads, and I guess that's one of the reasons we had five different talks on paroviruses at the 1983 workshop. When we organized it, we simply didn't know what was causing AIDS.

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 theories?

Wyatt: Amyl nitrites were discussed. I can see that just looking through the summary that I prepared seven years ago. It's not edited but we talked about—well, here, "Other factors might also play a role; however, its 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. So, we were clearly looking for not only agents but also 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 were increases 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 provided, he talks about how amyl nitrite, affecting vascular permeability, could perhaps render a non-pathogenic agent, given a different situation, allow for a different pathogenic pathway. So, I could see why it was a viable theory to keep alive until you had something better going.

Wyatt: It's an interesting chapter. And it hasn't been that many years ago—when you stop and think about it. A lot has happened since.

Harden: Thank you very much, Dr. Wyatt.

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