Walter, William 1995

Dr. William Walter Oral History 1995

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This is an interview of Dr. William Walter, who played key roles in the grants-funded areas of the NCI, taken on April 21, 1995. The interviewer is Dr. Carl G. Baker, former Director of the National Cancer Institute.

Baker: Bill, before we go a little further, would you give us a little bit of your background and where you went to school and so on?

Walter: My undergraduate degree is from Indiana University and I have a Bachelor of Arts degree in chemistry. And my medical degree is from Indiana University School of Medicine, and I have a Master of Public Health Degree from Johns Hopkins School of Hygiene and Public Health in 1951. I started out in the Public Health Service in the Venereal Disease Control Division, and I came into the Cancer Institute because I had expressed an interest in cancer epidemiology. And my first activity in the National Cancer Institute was in the epidemiology of leukemia and Hodgkin's disease, mainly in geographic distribution and time trends, epidemiological studies. In those days I was interested in the epidemiology of cancer, but not in the way we were doing epidemiology. It took me almost a year, for example, along with a statistical clerk, to gather information to get standardized mortality ratios from the 1950 Census and from States' Death Records, and so on, in order to do a simple study of geographic distribution of leukemia deaths. So, it was about a year between the time I started and I was able to publish something on leukemia mortality. And another year before I was able to get sufficient information to publish, along with a fellow named Sandy Gilliam, a study on time trends in leukemia with special reference to atomic testing in the western part of the United States.

Baker: Was this slow because you didn't have the mechanism set up for collecting and analyzing a lot of detailed data? You had to do it probably yourself?

Walter: Yes and no. I had a statistical clerk who was assigned to me full-time but, in order to get the raw material, and with the instrumentation that we had available, with our calculators and everything, it took a long, long time to get information to a point where you could utilize it and publish it. It was quite different from all my training in medicine and in public health to spend so much time on statistical manipulation and to take so long sitting at a desk and doing calculations and so on, that I was just ready to do something else afterwards. And that's why I went down to M.D. Anderson to become Medical Officer in Charge of a lung cancer project at M.D. Anderson, and then up to Women's Medical College, in Philadelphia, on a cervical cancer project. And then I came back to Bethesda, in Extramural Programs, when Congress appropriated some funds for some construction for specific cancer activities.

Baker: This was with Ralph Meader then?

Walter: With Ralph Meader.

Baker: When you were doing the epidemiology in cancer with Gilliam, was Shimkin the head of the Field Investigations and Demonstrations Branch?

Walter: Shimkin had Field Investigations and Demonstrations Branch. Epidemiology was a Section in that Branch. And what I did was, I went from the Epidemiology Section to the Field Investigations Section, where I thought there would be more action that would be more suitable to what I wanted to do. And then I left that branch and went into Extramural Activities, when Extramural Activities started doing things aside from just project grants that were more cancer oriented in developing activities that were suitable for enlarging the scope of cancer programs in universities and medical centers.

Baker: So, that was with Ralph Meader who was head of the Grants Administration?

Walter: Ralph Meader was head at that time, and then I came in.

Baker: The Grants and Training Branch, I believe it was called, in those days.

Walter: The first thing we did is we had a $5 million dollar appropriation--I think it was fiscal year 1960--for construction. So we had to review construction grant proposals. The funds were available for only the year that the monies were appropriated. And by the time the funds became available, that was like in February of 1961, we started the review, and we had to have everything completed by June 30th of '61.

Baker: That gave you some different experiences than you had before?

Walter: Yes. The Division of Research Grants threw up their hands and they said, "We can't review these things," so we had to do the review, write the summary sheets, take the applications to the Council.

Baker: Time was a difficult parameter to get people cleared and on board for a committee review too.

Walter: Yes. The one construction project that probably amounted to something was the McArdle Laboratory at the University of Wisconsin. Other than that, those funds went to things that didn't really promote cancer research very much.

Baker: Why do you think that was?

Walter: I don't really know. I think some of the activities later turned out not to be particularly cancer oriented. We had one project up at the University of North Dakota, in the Biochemistry Department, which turned out to be non-cancer.

Baker: But you had a review group that supposedly reviewed on a basis that included cancer relevance, I presume?

Walter: The review group was strictly *ad hoc*. We did review at the time of the site visit. We site visited every application and we'd get reviewers to come in and do a site visit and make a recommendation and, from that, I would write a summary sheet and take it to the Council, and the Council would recommend it, or not recommend it. Everything that we recommended, the Council went along with. We did have a project at the Wistar Institute in Philadelphia which was cancer related.

Baker: Well that, and McArdle, are at least cancer related.

Walter: And then we had another one up at-- You see, the City of New York had a cancer hospital, and we approved a construction project for that and it was later--two or three years later--it was folded into Sloan-Kettering, so that might have been a good cancer project.

Baker: Emory University had one of these, I believe.

Walter: Emory University was just a general one.

Baker: Because I had an interesting experience later in this regard when I had made a site visit on another grant proposal from Emory and found out that the building we were in was constructed with the $5 million dollar construction funds that you're talking about, I went through the building and they were teaching undergraduate English, etc., and I couldn't find any cancer work. So I came back to Bethesda and proposed that we ask Emory University to give the money back. Of course, I didn't get very far with that. Boisfeullet Jones was the Assistant Secretary of Health, or some similar position, and formerly-- I forgot his position at Emory, was he Vice President of the University?

Walter: He was on the Board of Directors or something.

Baker: So anyway, that didn't get very far as a proposal. A couple of things on your experience before you came to the Cancer Institute. What kind of assignments did you have in the Venereal Disease Control Division?

Walter: Most of my time in Venereal Disease Control was spent as Director of the Venereal Disease Control Division in Florida. And I had been at Johns Hopkins, and then I was sent to Florida as Director of Venereal Disease Control. And during that time the Venereal Disease Control Division was under the Associate Director for Preventable Diseases but, for some reason, the Director of that activity had to leave town and there was a lot of activity in the Bureau of Preventable Diseases and I was the only one around to take his place.

Baker: Were you in Miami?

Walter: No. We were in Jacksonville, Florida. And so, the Director of the State Health Department appointed me as Associate Director of that Bureau in addition to being the Director of the Venereal Disease Control Division. And the VD people in the Public Health Service weren't too happy with that because my activity in venereal disease was diluted because of my general duties as Preventable Disease Bureau Chief in the absence of the other guy.

Baker: How would you have liked to have had the AIDS situation?

Walter: Well, at that time, the main activity that we had was the polio situation, because that was before the Salk vaccine or the Sabin vaccine, and there was talk about the -globulin, and we were inoculating-- Well, we were predicting where the epidemics might occur. And if we thought that there would be a big epidemic, we would go down and we would inoculate children.

Baker: You mean with antisera?

Walter: With -globulin, in order to head off this. And so I was doing mostly that kind of stuff, aside from the VD work, and that didn't sit too well with the Public Health Service Venereal Disease Control Division people.

Baker: Yes. You were caught in the middle.

Walter: So I was caught in the middle. And so when NIH exhibited some interest in my coming up with Mike Shimkin, they were happy to let me go and I was happy to go.

Baker: After you came with Ralph Meader you had a great variety of assignments between that time and your retirement from the PHS. Do you want to give us a quick rundown of some of the activities?

Walter: Well, starting out, when I came into Extramural Activities, basically the prior history of the program was that it was strictly a project grant program.

Baker: They became known as R01 Projects.

Walter: R01 projects. And there would be projects that would come in that would be assigned to the Cancer Institute, and they would be reviewed by the Division of Research Grants Study Sections. Then they would come up before our Council. And I remember the Council would meet and the Executive Secretary of each Study Section would come before the Board and would defend the action recommended by the Study Section.

Baker: Before the Council, you mean?

Walter: Before the Council, in those days. Well, that was most of the activity. And then, when I came on board, the Congress had just appropriated some monies for construction of cancer facilities on a non-matching basis. NIH, before that, had construction money, but it was on a matching basis, where the state or university or institute would have to put up 50 percent of the money, but for Cancer we were able to put up 100 percent of the money. Also, during that time, the Congress gave Cancer the authority to support, in addition to research project grants, program project grants, and so-called clinical center grants. So, it was kind of like a time of transition in the Cancer Institute.

So, my first assignment in the Grants Program was with the construction, because, as already mentioned, that was the most acute thing that had to get done because we had $5 million dollars for one fiscal year only and we had to get that money spent.

It turned out that we had more grants approved than we had money to spend, so Congress appropriated another $5 million dollars and the ones that we approved the first year, we just funded the second year; we didn't go around and review any more construction grants. We just approved the ones that we hadn't funded from the first round.

Baker: Do you know the origin of the clinical centers grants?

Walter: Well, there had been a Clinical Center Program at NIH in the General--in the--

Baker: That came later. The Cancer clinical center grants were the initial ones at NIH, and other clinical center grants from NIH came after that.

Walter: What do you mean?

Baker: Well, there was general clinical center grants for NIH as a whole, but that came after the Cancer Institute had already sort of pioneered the clinical center grants. And do you know how NCI got into that?

Walter: No.

Baker: Well, Sidney Farber was the one who was talking about the need for clinical cancer centers, basing it on generally the idea of what he had in the Farber Jimmy Fund supported Children's Cancer Center in Boston, but enlarged for other forms of cancer. And the Senate Appropriations Committee, listening to Sidney Farber's testimony, wrote into the bill that the NCI was to come back the following year with a plan for clinical cancer centers. And a month before it was time to present before the Appropriations Committee, I was Assistant Director with Rod Heller then, and I said, "Rod, we're supposed to have a plan before the Appropriations Committee on clinical centers grants." And he said, "Fine. Write up something on that." So I wrote up the proposal for what a clinical center was and later I got the job of chairing the committee that Shannon set up to advise on general clinical center grants. And so Farber played, I think, a key role again in initiating that, and Congress was really the one that got the NCI, I think, into that, as they did in the Chemotherapy Program.

Walter: That's right. Actually there were two programs that were set up after that. It enlarged on the R01s, or the so-called research project grants, and we called program project grants PO1s, and P02s were the clinical center grants. Now, the P01s were grants in which there was no clinical component. And we could do some construction or remodeling of facilities under those grants, but there were some restrictions and I don't recall right now what those restrictions were. On the P02 grants we could remodel up to an unlimited amount of money. In other words, we could go into a hospital and remodel a part of that hospital as a clinical center and spend any amount of money we wanted to. No restrictions. And that was basically the difference between a P01 and a P02. In a P02 grant, or the clinical center grants, we had no limit on the amount of money we could spend on remodeling in order to provide clinical facilities. But, in any event, in the early '60s, the Grants Program really started dealing with cancer programs that were really cancer-oriented through program projects and through clinical centers.

Baker: And multidisciplined and both clinical and laboratory, and the objective of the centers grants was to integrate the different disciplines required to have a full program on cancer. And this also attempted to stimulate information transmittal from the cancer center to the practicing physicians and others in the community, as I recall.

Walter: That's right. And I think they've done a good job, although lately they might have fallen into some disrepute. I don't know. I've been out of it long enough to not be in close contact with what's going on.

Baker: And this takes us up through the period when Ralph Meader was retiring from this position, or was there other things before he left?

Walter: You see, actually, Ralph was a research project grants man.

Baker: He certainly was a friend of the individual investigator. As you know, we worked at night a lot, and he would get telephone calls from all over the country, not only seeking advice from him on their grants, but on personal matters as well, and there was no greater friend of the grantee than Ralph Meader.

Walter: That's right. So, in many respects, he was a very conservative grants person. And although under his watch Congress passed these broader programs beyond the research projects, or R01 grants, he kind of got into that, I wouldn't say reluctantly, but he didn't quite know exactly how he was going to pursue it. Following him Phil Walkies came in and Phil was good in that he delegated a lot of activities to many of us and we could do pretty much what we wanted to do.

Baker: Were there some new forms of grants that came in during that period that you were involved in?

Walter: There weren't really new forms. We still had the P01s and the P02s and the R01s. But, you see, Ralph Meader had no organization at all. He had one individual, I think, working with him, and I forget his name. You might remember.

Baker: Yes. Malcolm Ray. He had been with the American Cancer Society Committee on Growth.

Walter: But he had no organization at all. The Grants Program was Ralph Meader and this one other individual. When Phil Walkies came in, he decided there had to be some kind of an administrative organization, so he sent around a memo asking for any ideas about how we could reorganize the Grants Program. So, I sent up a memo saying what we ought to do is have at least two branches. We could have one branch that dealt only with R01s or program grants that go through DRG, and another branch which dealt with activities that didn't have any specialized activities, such as training, and centers, and program projects, and construction, and clinical education, and at that time we had the Research Career Awards and Research Career Development Awards, i.e., all of those things that were not specifically amenable to going through a study section.

Baker: You mean discipline oriented projects would go to one Branch and the other projects would go to the other Branch?

Walter: Yes, discipline oriented in one Branch. The completely undisciplined activities would be in another Branch, and I would head that Branch.

Baker: I don't think you should call it "undisciplined."

Walter: That's what I called it. Anything that did not fit into a disciplinary category, with the exception of a couple of project grant programs that I was particularly interested in, and we would keep all that in this one Branch. The ones that I mentioned in particular were epidemiology--there was an Epidemiology Study Section--Medicine and Surgery Study Sections, which I kept. The Chemotherapy Study Section projects would also be in our Special Programs Branch, as I called it.

Baker: Well, it sounds like you were proposing to take everything except a few grants, except the number of those RO1 grants was still high in number, so the quantity of work was still heavy in the R01 grant area.

Walter: You see, the Cancer Institute had a lot of grants that went to study sections, and I know you used to question, "Well, what's the cancer relevance of many of these things?" and if they were looked at, many would say, "Well, basic research, in cancer you have to have a lot of that. Maybe you can't see it, but it's there." There were things in biochemistry--

Baker: You had to have a broad definition of cancer research, all right. But I remember Bob Berliner, one time, couldn't understand why I didn't want to fund a project that was clearly in some other institute's bailiwick because it had a 100 priority score, and I said, "Yes, but the other institute ought to fund it." "Well, but he got a 100 priority. How could you not fund it if he got a 100 priority?" And that was an interesting philosophy that was widespread, of course. It still is, I guess.

Walter: Well, with some of the project grants that I took, that's right. The Epidemiology Study Section had very few grants that were cancer grants, so that wasn't a big load. And the same is true of the Surgery and Medicine Study Sections. I also kept Cell Biology because there were not very many grants.

Baker: Gee, there should have been a lot of them.

Walter: I was so ignorant about cell biology that I got along well with the Executive Secretary and the Chairman and they would invite me to their site visits, so I just kept that one because-- I wasn't a threat because I didn't know anything about it.

Baker: That's an interesting idea about being a threat, but you're right, those factors enter in.

Walter: Yes. And I think I kept virology too because we didn't have very many--

Baker: Well, I wanted to go into that one next to lay some groundwork for an additional interview here.

Walter: Well, I did keep virology.

Baker: There was a study section called Virology and Rickettsiology Study Section, the V&R Study Section we called it.

Walter: The Virology and Rickettsiology Study Section.

Baker: Was Scudder the Executive Secretary of that about this time?

Walter: No. Scudder had left.

Baker: Oh, had already left?

Walter: Uh-huh. And the Executive Secretary was a fellow named Lauri Luoto. Lauri Luoto was a veterinarian.

Baker: How do you spell that?

Walter: He's Finnish. L-A-U-R-I, L-U-O-T-O.

Baker: Oh, yes, yes. Now I remember. Now that I get the spelling. Yes. He was a nice guy.

Walter: Actually, Lauri and I got along quite well, and that's another reason why I kept the Virology, because we didn't have many grants come through there related to cancer. And at that time one of the members of the study section who was involved in cancer activities was Richard Tjalma, and he was a member of that study section.

Baker: Yes. Another veterinarian.

Walter: Yes. He was a veterinarian.

Baker: And he became one of the Assistant Directors of NCI later.

Walter: He was an Assistant Director and he's now retired.

Baker: A colorful fellow and a wonderful story teller.

Walter: Yes. And Lauri Luoto later, actually, came to work in the Cancer Institute as Head of the Virology Program in the Cancer Institute.

Baker: Which Virology Program?

Walter: The Virology Grants Program. And Lauri later retired and went to Colorado State University in-- I forget where. Wherever Colorado State University is now.

Baker: Boulder, I think.

Walter: No. That's the University of Colorado. This is Colorado State.

Baker: Fort Collins.

Walter: They have a Veterinary School at Colorado State.

Baker: Can we go back to when Scudder was Executive Secretary of that study section, because he considered that that study section and their activity and his activities created a Cancer Virology Program. And when Endicott set up the Special Viruses Leukemia Program, some of those projects were moved into the program area which utilized contracts for support. Scudder was not very happy about that transition because he felt the program that he'd worked hard with the study section to set up was taken from him and moved over into another part of the Cancer Institute, and he wasn't too happy about that, I found out later.

Walter: Well, that may be true. The fact of the matter is that within the Cancer Institute, in the Grants Program at that time, any link between viruses and cancer was not looked upon sympathetically.

Baker: Certainly early it was not.

Walter: And so the Grants Program within the Cancer Institute, was not active in pursuing activities involving viruses in cancer.

Baker: What do you think brought about a change in the philosophy of whether viruses should be looked at more actively in leukemia and other cancers because there was a shift around 1953. Well, the Program, the Special Virus Leukemia Program, was started in 1964. One reason the dates on the questions sent to you start at 1950 is that prior to that hardly anybody was interested in doing any work on viruses in cancer, but we had a shift in philosophy and all of a sudden you had a blossoming of the investigations, whether they were grant funded or contract funded, in cancer, first leukemia, and then that quickly spread to other cancers as well. So, from your standpoint, what do you think brought this change about?

Walter: What do I think brought the change about? I think it was brought about primarily because of the activities in the Cancer Institute itself. Certainly in the grants area we didn't do anything. We were dragging our feet and, as far as I know, the Grants Program never did take a leadership role in this area. We were always being dragged along, I think.

Baker: Of course, I'll take up for the grants area in reminding you that Howard Temin and David Baltimore were both funded with grants, although Baltimore also had some support from the contract side, and certainly he had resources that were put together by the Program which were not available before.

Walter: Well, yes, Carl, that's true. But the people that were funded through grants were quite well known prior to any activity that they were doing in cancer virology.

Baker: Do you mean from polio primarily?

Walter: Yes. And so I always looked on it as the fact that they were being funded, not because of what they were doing in cancer activities, but because of what they had done and because of their expertise in virology associated with activities aside from their interest in cancer, *per se*. If you look at the things that would get through the V&R Study Section, or the individuals who would get recommended for approval, many of them were well known virologists from previous work. In those days, you know, almost anything that was recommended for approval could be funded.

Baker: Yes. It's quite different now, isn't it?

Walter: It got to be so that you'd have to make a special effort to fund the low 10 percent of recommended grants. And the grants that the V&R Study Section recommended for approval, that dealt with cancer virology would be recommended, but not with very high priority scores.

Baker: That was part of this feeling that viruses had little to do with cancer in those days.

Walter: That's right. So you get the feeling that they were recommending them for approval kind of reluctantly and not with high priority scores but with mediocre or average priority, or less than average priority scores and we would fund them because we were funding everything that was approved. So, even though the study section would approve many of these people that were involved in virus in cancer activities, they were approving them because of their stature in the field, and not with enthusiasm.

Baker: Yes. Well, this last discussion gets us into the first question about what were some of the key scientific findings that took place that also, I think, accounted for this shift from no interest in cancer virology to the beginning and blossoming of the whole area? And I'll give you a hint of my views, that the Ludwig Gross findings that leukemia could be induced by cell-free extracts was a key finding, but nobody believed him for at least a couple of years before they could confirm it, and during that time Sarah Stewart and her polyomavirus created a new excitement in the viruses cancer area. And once Gross's work and Sarah Stewart's work were confirmed, a new interest in cancer virology became part of the picture. Do you see that, that way, or were you too far removed from that? You see, Gross was in the VA Hospital, and so he didn't have grants.

Walter: He was up in the Bronx, or somewhere, wasn't he?

Baker: Yes. In the Bronx. The VA Hospital. And he was funded through VA funding. He wasn't a grantee. And Sarah Stewart, of course, was intramural.

Walter: Yes. I mean, you know, I think you're asking the wrong person for this because my knowledge of this area is very small, and I have an abysmal ignorance about virology in cancer. And I guess it's because I wasn't intimately involved.

Baker: Yes. You were in a different area, so I don't expect you to have followed the details.

Walter: --and not only that, but the exposure that I had led me to have a lot of questions about the validity of the role viruses played in cancer in any event. I mean, I was exposed to people who had a lot of questions about whether or not any of this was actually important, or not important. And we in the Grants Program, I must say, we never really pushed hard or followed any of these scientific activities.

Baker: Do you recall in '64 the initiation of the Special Virus Leukemia Program?

Walter: Oh, yes. I recall that. But that was outside of our area so it was, "Okay, go ahead and do it."

Baker: You didn't feel it was something to object to necessarily?

Walter: Well, we didn't object to it.

Baker: Some people did.

Walter: You could do what you wanted to do. Just leave us alone.

(Laughter.)

Baker: So you probably don't have a very good idea of how that all got started?

Walter: I have no idea of how it all got started. It's just that, you know, if you want to do it, go ahead and do it, but--

Baker: I like to think the key decision was made by Endicott to seek an additional appropriation, a special appropriation, for that program. And Bryan, Rauscher and I, with Zubrod also reviewing, put together information to justify Endicott's wanting to seek a special appropriation. And Shannon insisted on having a good layout of the evidence on why you think that's justifiable, and so we not only put together that memo which Endicott sent to Shannon, but Shannon wanted some more information when I happened to be Acting Director at that time, while Endicott was away, and so we put together some more information for Shannon. And then he said, "Okay, go and seek the money," and Congress then voted a $10 million special appropriation which, in those days, looked like a lot of money, and I guess it was. I still think $10 million is a lot of money.

Walter: And especially in those days it was a lot of money.

Baker: Yes. So, after the Congress approved this, Endicott came to me and Carrese and said, "Okay, you guys have been talking about planning. Plan me a program of $10 million dollars for a viruses-cancer area." And then Rauscher, Carrese, and I, took 3 weeks off, disappearing from the telephones and all, and laid out the plans for the Special Virus Leukemia Program. And then, a short time later, Zubrod, Shephartz, Carrese and I laid out the chemotherapy systems plan. So these are the key steps in the origin of the Special Virus Leukemia Program, which was later changed to the Special Virus Cancer Program, as it became evident that a lot of solid tumors, in animals at least, were virally induced. In fact, we got up to over 200 virus isolations that produced tumors in animals and yet, as you know, the struggle to find human viruses is still a difficult area, although AIDS is making a big difference as well.

Walter: Yes.

Baker: Do you remember when this Special Virus Leukemia Program was presented to the Council, with the big charts that we put up?

Walter: I think sometime in 1965, or '66.

Baker: I think it was 1965.

Walter: Yes. 1965. Yes.

Baker: You were there, at the Council meeting, when this was presented?

Walter: Yes.

Baker: Do you recall your reaction to that?

Walter: Well, our reaction to it was, "Fine, go ahead and do it." You see, this was something that wasn't going to involve grants; it was going to involve some contracts and some intramural people, and that was good, if you wanted to do it.

Baker: But we all know that a lot of your academic scientist grantees objected because they would rather have the money in grants.

Walter: Well, yes, but they went along with it. They wanted to have the money in grants, but I think there would have been a problem: the study section probably would have approved many of the grants with a priority that was not enthusiastic.

Baker: Well, I don't think the study sections favored the planned approach, because way back in 1959 I met with the V&R Study Section in Atlantic City and presented some ideas on an integrated planned program to tackle leukemia and I got a really cold shoulder, of course, because that was planned research and the independent investigation was the way activities should be pursued. So, as I look back at the slide I presented at that meeting, if you turned it at right angles, it was a simplified version of what became the Special Virus Leukemia Program Plan. But it was not very acceptable to most academic scientists--it never was--in the view of a lot of people.

Walter: Well, that's right. I don't know how it is today, but I think the V&R Study Section would still be dragging their feet in this area as far as I know.

Baker: So you personally weren't against a planned program utilizing contracts.

Walter: We had one area where we were able to fund one of the people, and that was Joe Melnick, and I don't remember exactly what Joe was doing, but Joe was an individual who received a program project grant. It didn't go through the Virology Study Section. It went through our own committee. And so, to that extent, that was about the only extent that the Grants Program ever got involved in virology.

Baker: Well, Melnick, of course, came out of the polio area, and he was primarily, in those days, looking to assay specimens from humans by purifying them with virological technology and introducing them into various primates. And so he was concerned with primate production as well as the virology techniques involved in assaying and searching for viruses, both in the primates and in humans as well. And Joe was another dynamic individual who was always looking out for ways to get funding for his activities. So he not only participated through the program project channels, but also in the Program funding with contracts. But he was an effective guy. He also was a very good adviser. He spent a lot of time with us, advising on what should be done, along with Sabin and a few others who were quite good on both committees and as individual advisers.

Walter: You see, we, in the Grants Area, as things went on, we were--or at least I--was more and more involved with cancer institutes and cancer centers, and the established cancer institutes, such as M.D. Anderson and Sloan-Kettering, the Institute for Cancer Research in Philadelphia, and the cancer center grants that we had, the activities in those areas were not involved in anything to do with viral etiology of cancer or the association of viruses and cancer. The major cancer institutes, at M.D. Anderson Hospital, they didn't have an vital, active virus program.

Baker: Not until later. Yes.

Walter: Nor did Sloan-Kettering, nor did the Institute for Cancer Research in Philadelphia.

Baker: Well, Charlotte Friend was at Sloan-Kettering, and she was pretty active, but again, not necessarily only through the grants.

Walter: Yes. And so we were not really exposed to very much activity in these areas that you're talking about.

Baker: But you would hear summary reviews periodically before the Council?

Walter: Yes.

Baker: But you had your own worries.

Walter: Yes. We would kind of listen with one ear.

Baker: Yes. You were worried about what you had to present on your things, so it distracted you from really closely being immersed in this at all.

Walter: It really didn't make a deep impression on many of us. We were concerned about things that were coming up. For example, in those days Henry Kaplan was a member of the Council, and we were starting to get into radiation therapy activities and radiation therapy training programs, and attempting to work with Henry in separating radiation therapy from general radiology or diagnostic radiology.

Baker: And then the training. He had a good positive effect by getting needed training and quality control on radiotherapy units around the country.

Walter: So, we were involved in things of that nature and more concerned with those activities, or at least I was, than we were in some esoteric activities of viruses and cancer and all this kind of stuff.

Baker: My impression though was that Ralph Meader really objected, as so many academic scientists do, to the idea of planned programs in biomedicine. Did you have that impression from Ralph?

Walter: Yes. And, of course, we didn't have any planned programs in cancer--I mean in grants. They were completely unplanned--

Baker: *Ad hoc.*

Walter: *Ad hoc-*,investigator-initiated--

Baker: Well, not completely, because you laid out some of the guidelines for some of these larger projects, and I would call that a form of planning. But they didn't integrate the various ones.

Walter: But that was later on. Ralph had left.

Baker: Yes. Well, you know Bo Mider objected to this approach too intramurally.

Walter: See, we were able to lay out some plans-- After Ralph left, Phil Walkies came in, and Phil didn't push anything, didn't object to anything--

Baker: But he asked you to at least think about other things?

Walter: That's right. And--

Baker: At least he asked, right?

Walter: Yes. Another thing that came up during Phil's time that we got involved in was the so-called "heart disease, cancer, stroke" activities that the Congress was interested in and, as a result of that, the Cancer Institute got money for planning grants.

Baker: Yes. For the institutions around the country to do some planning.

Walter: Yes.

Baker: Because the Congress did favor some planned approaches.

Walter: So we grabbed a hold of that money for planning grants, for planning, and started planning cancer centers with that money.

Baker: Well, that's what the Congress wanted done.

Walter: And so, we were involved with a lot of other things, aside from the viruses and leukemia and stuff like that.

Baker: Sure. From your perspective that was perfectly appropriate.We mentioned a few people, like Melnick and Chuck Evans. Does anybody else come to mind who was very helpful on committees that might touch on the viruses cancer area?

Walter: The only-- No. The only name that comes to my mind is Sol Spiegelman, and I don't know how much of a role he played in this.

Baker: Well he was, again, influential on both committees and as an individual adviser.

Walter: I think he was from Columbia, wasn't he?

Baker: Right. He ended up heading the Cancer Center at Columbia. He died prematurely. I think a heart attack. I'm not sure. He was a very imaginative guy, moving rapidly, published a lot, and ended up being slightly on the wrong track, but that didn't matter because he was very stimulatory in his publications and the questions he raised and sought data on. So, he was certainly one. Let me shift this a little to political figures. Any political figures come to mind that were influential in those days?

Walter: Give me some hints. I can't think of--

Baker: Well, Sidney Farber is a scientific politician, or a medical politician, who certainly was influential. And Mary Lasker. And, of course, in the Congress we had the heads of the Appropriations Committees.

Walter: Lister Hill and--

Baker: Fogarty.

Walter: Fogarty.

Baker: How about anybody from the American Cancer Society that you recall being-- You know, they always had somebody that came to our Council meetings.

Walter: Yes, but I can't recall names.

Baker: Harold Diehl. Well, names are the hardest thing to recall, other than dates.

Walter: We also had a fellow from--well, it's now the Nuclear Regulatory Commission--who used to come to our Council meetings, from the old Atomic Energy Commission, the medical director of--

Baker: Yes. He was a radiologist from New England Deaconess.

Walter: I can't think of his name.

Baker: Shields Warren. We can shift to the sixth question, which gets into the area of resources, and we're talking about tissue culture cell lines, virus preparations, antibody preparations, animals and other supplies. And the question that I want to get at deals with the situation back, say, in 1960 compared to later. Did the Viruses Leukemia and Viruses Cancer Programs change the availability of quality controlled resources in sizable amounts compared to the period before the program started? It's a loaded question, perhaps.

Walter: It might have, but I don't know. I mean, to my knowledge-- We were kind of so far removed from activities that--

Baker: Well, but today you can commercially buy a lot of this stuff, which you couldn't in 1960, and there were several contracts that really were to produce quality controlled resources in large amounts, which were then made available to participants in the Program and to other qualified investigators. And I think this laid the stages for some biotechnology today, but maybe you don't agree with that?

Walter: Well, I suppose so. You know, early on though Frederick wasn't even active. I think it was when Rauscher was Director that President Nixon declared an end to biological warfare.

Baker: It was before that because Rauscher and I and Zubrod briefed President Nixon on the Cancer Program the day he announced that he was switching it from the germ warfare to the cancer area, and that was a little bit before I was no longer Director.

Walter: Okay.

Baker: But, by that time we had very active contracts though in producing sizable quantities of needed resources. And a lot of this was developmental research, and we didn't even have good animal husbandry data on blood counts on primates for example, and so we put developmental money into that. And tissue culture, before the Program got started, we didn't even know how to freeze and thaw tissue culture cells so they would consistently revive. We put developmental research money into determining the conditions that will optimize that kind of freezing and thawing of tissue culture cell lines. There were many problems on quality control on tissue culture cell lines available. And I joked with the people coming out of the polio area that they were very good when they found a new isolate of a virus, or some assay system, of exchanging samples with each other to check on the validity of the findings before they published, however, by the time they had finished distributing samples to their colleagues they didn't have any left to work with, and therefore we needed much larger amounts. Many of those people said, including some of our NCI staff, "You can't trust industry to make good quality materials." And I said, "Well, you don't have to use it if your testing, by whichever way you want to test it, indicates that it's no good, we don't expect you to use it. But we can put the same quality control requirements here as you would want if you were making it." And I knew I got over that hump when Moloney came in one day and said, "That Pfizer contract," he says, "They've got stuff that's as good as anything we ever made and they've got buckets of it." And we finally got the investigators to accept the idea that industry could make good stuff in quantity.

Walter: But those are activities that are certainly essential and that can be promoted through contract activities, and again they're not going to get anywhere through a grant study section.

Baker: Yes, because it wasn't research.

Walter: That's right.

Baker: And we, therefore, had fewer objections to our resources contracts than we had for research contracts.

Walter: Yes. But neither one of them was going to get anywhere through the Virology Study Section. I mean, even though individual virologists who might submit grants would utilize the resources, but in order to obtain the resources and to make them available, that kind of activity would never get through a study section.

Baker: So, my point was we needed both kinds of things, not "either/or," even though there are a lot people arguing, you know, it ought to be one way or the other. No. Some things you can do better with grants, like exploratory research, and I'll defend strongly the grant system. But for, as you say, developing some of these other things, it's not suited.

So, the question is, did we really accelerate progress by making quality controlled resources available? Again, I think it's a loaded question, but--

Walter: Sure. Certainly.

Baker: And I'm not sure there is a widespread appreciation in the academic community of the role played by the Program and the value of these things.

Walter: Well, again, I think you're absolutely correct on that score. It's just taken as a "gimme," that these things are now available and that's it.

Baker: So, since you were not in the middle of this, you don't have a good grasp for who made the key decisions for this sort of development?

Walter: No. I don't know. Do you remember the American Type Culture Collection?

Baker: Yes. Stevenson was the head of that for several years.

Walter: Really, the only thing that Grants ever did was we kind of supported that thing with a small grant.

Baker: Well, there was a construction grant which was very important in getting that American Type Culture Collection function out of a firetrap frame house in downtown D.C., to get a nice brick building in Rockville, and I, fortunately, played a role in that when I was with Ralph Meader. It seemed to me here was this tremendously valuable resource for the nation, or the world, and it was in a firetrap which had the chance of destroying a tremendous number of standardized bacteria and fungi strains, and we were just beginning to get tissue culture included in that function. So, some of the construction money helped make that transition, which I thought was a very important thing.

Walter: Yes. But there again, it's--

Baker: It's different from the other stuff.

Walter: Yes. At the moment I don't recall what grant support was available.

Baker: Bob Coghill, who was with Zubrod in the Chemotherapy Program, also got industry to kick in a good bit of money to help build that brick building in Rockville.

Walter: But, I mean, we used to support it as an ongoing activity.

Baker: Well, they did research functions too, so they had some research project grants they proposed which got funded. They still do.

Walter: Yes. But it was mainly looked on as a resource to supply microbiological items.

Baker: They didn't think it was research, but there were some projects that were put together as research proposals that got funded as research. Yes. But the construction thing was unique. Okay. Number seven. Do you have any feel for the relative amounts of funding of viruses cancer work funded through grants compared to those activities funded through contracts? Most people don't. We'll have to look up the figures. But it was clear that the contract funds grew much more rapidly than the grants funds for viruses cancer work.

Walter: That's right.

Baker: And I'm partly guilty of that, if you want to look at it that way.

Walter: Yes. We would just take whatever the V&R Study Section would recommend and we'd fund it, and that's it. They would recommend for funding, again not with a very high priority, or not with a great deal of enthusiasm, but usually the thing would be, "Well, he's a pretty good virologist. We can't disapprove him," in other words. And I think back to those days of the V&R Study Section when Harvey Scudder was not unsympathetic towards cancer activities, and I know Lauri Luoto wasn't. But, by and large, most of the requests that would come in to them would not be for research that was cancer-related and my only recollection of anybody who was doing anything in viruses in cancer was again with Dick Tjalma, who was working with Burmester at Michigan State. And I don't remember whether he was in the Cancer Institute before he went there or not.

Baker: I don't think so.

Walter: But then he came to the Cancer Institute after that.

Baker: Yes.

Walter: But he was working with something--I don't know--chicken viruses, chicken sarcoma, or something. I forget.

Baker: Well, you're expressing one of the problems, I think, between a categorical Institute and the Division of Research Grants' philosophies, and there is a continuing problem of how you relate the excellence in a scientific discipline to the categorical relevance. This is an age old problem. And at one extreme end you have people, usually academic basic scientists, who say, "Relevance, you can't tell; you have to give the investigator a free hand to pursue whatever he wants to do," and, on the other hand, you get people who are interested in solving disease problems who say, "Yes, we've got to have a lot of basic research, but how do we get things accomplished that are more directly relevant as well?" And this brings up the concept of the Organ Site Program, because these were started partly because there was no study section that was approving anything on large bowel cancer, and when I became Director there were only nine grants, totaling $212,000, on large bowel cancer, which is one of-- Well, if you put male/female statistics together, it's the most significant cancer we have, and yet we only had nine project grants on it. So, how to get work going on that, and bladder, and prostate, was what led to the idea of the Organ Site Program. Do you want to comment on that?

Walter: Well, my only comment about the Organ Site Program is remembering, by that time Phil Walkies had left as Director of the Grants Program and, because of your willingness to utilize whatever mechanism was available in the Cancer Institute to get things done, the Grants Program was able to expand, and actually the name was changed from the Division of Research Grants to the Division of Cancer Research Resources and Centers, and "Grants" was left entirely out of it. We didn't even have a-- The "Grants" name was not even in it. It was the Division of Cancer Research Resources and Centers. And I remember when you-- Palmer Saunders was the Division Director, and you brought us in and you said, "Is it possible for you to support, with grants, some designated programs in organ site activities?" And I remember you specifically mentioned at that time large bowel and prostate. And we said, "Sure, sure, we can do that." I think we said that anyhow.

Baker: Well, I was glad to hear your answer.

Walter: We went up to your office on the top floor of Building 31 for you to tell us that. And we came down to our offices on the tenth floor, and Palmer said to me, "Okay, draw up the guidelines for this."

Baker: It sounds like Rod Heller and me with the Cancer Clinical Centers.

Walter: So, I remember I drew up guidelines for the Organ Site Program.

Baker: Yes. You were great on drawing up guidelines.

Walter: And we presented them to the-- Well, first I gave them to Palmer and he said, "Is this all there is?" And I said, "Yes, that's all there is." He said--

Baker: That's all you need.

Walter: That's all we need. And he said, "Well, okay," and then, with your O.K., so we gave them to the Council and they said, "Okay, let's do it." The first Organ Site Program was the Large Bowel Program, and we were going to put the coordinating office down at M.D. Anderson. And the head of that was going to be a surgeon named Walter Burdette.

Baker: That's right. He was also a geneticist. He had a Ph.D. in genetics.

Walter: He had recently come from Salt Lake City. And the program hadn't been started yet, but there was a big cancer meeting at San Diego, and Lee Clark was down there and we were going to have Bill Ross, who had come over to us from the Cancer Control Program. Cancer Control had been disbanded.

Baker: Well, at NIH, first, Shannon threw it out, and then it died in the other part of PHS.

Walter: So there were some physicians that were--

Baker: That needed assignments.

Walter: That needed assignments, so--

Baker: Bill Ross was the one you got.

Walter: We got Bill Ross. As a matter of fact, I hired Bill Ross and Bill Roberson from those programs.

Baker: Well, you batted 50 percent, anyway.

Walter: So we got Bill Ross, who was going to run that program, along with the Career Awards Program with us. And so, anyhow, we met in San Diego at that big resort hotel down there, and Lee Clark was all for it, and Walter Burdette was going to arrive from there, and it got off to a shaky start.

Baker: Why?

Walter: Because of Walter Burdette.

Baker: Which he did what?

Walter: I forget exactly what he did.

Baker: I know what he did.

Walter: What did he do?

Baker: The first award that they made was for his own program, and that's a bad activity for a chairman, especially the first award, and so Lee Clark fired him.

Walter: Yes. And then that program got off to kind of a bad start because we later fired Bill Ross too, from our end of it. But I remember Bo Mider's wife was working for us then, Ruth Lyman. She had the Career Development Awards. Well, we also picked up some Cancer Control projects. You see, under you we were able to do everything, Carl. We really were.

Baker: Well, I didn't want Cancer Control, but the new National Cancer Act, which Nixon signed in December of '71, brought Cancer Control back into the NCI. And the first year then, I was bawled out because I only put $3 million dollars in it, but I had to take that $3 million out of the other part of the NCI budget since I wasn't given any funds for the Cancer Control activity. I had to carve it out of the ongoing budget. So, a lot of people in that area thought I wasn't doing enough with only $3 million but, as I say, we didn't get any money for that.

Walter: Well, Diane Fink--I don't know if you remember her--

Baker: Yes. She was the first one to head this activity up, I guess.

Walter: She and Bill Ross later got married, you know? It lasted about two weeks. But, in any event, when you were Director, we had Cancer Control, we had all the Career Development Awards, we had Training, we had Clinical Education, we had the program project center grants, construction grants, single instrument grants. We had almost everything.

Baker: I might make another couple of comments on the Organ Site Program, particularly Large Bowel. When I became Director I looked at the distribution of the grants and discovered this really rather minuscule effort in large bowel cancer, and so I asked a few questions around. "How come we have so few grants in this very important area?" And the answer generally was, "Well, we don't have any research leads." I went in the library and in about 3 nights I found out that we had a good animal model for large bowel cancer already in existence. You let me have an animal model, I can build you a program around it. And so it was clear that to me we just didn't have reviewers who were sympathetic to that area. So the idea was to create then, in the Organ Site Program, a group of good scientists, both laboratory and clinical, who were interested in the subject and then let the word go out that we were interested in receiving proposals, and that way then we got good proposals coming in and that group then recommended approval because they were interested and knowledgeable in the subject matter. The study section members just didn't happen to be in that area.

Walter: Well, yes. It wasn't a matter that people weren't interested, I mean that investigators weren't interested; it's that they didn't have an opportunity for their interest to be manifest. I mean, DRG is not set up to be cancer-oriented, or infectious disease-oriented, or arthritis-oriented, or anything-oriented, except for the disciplines that they have in their study sections. So, investigators tailor their work to fit into what the Division of Research Grants is. And then the Division of Research Grants would say, "Well, this looks like it might be cancer-oriented a little bit, maybe, so we'll give it to Cancer," or arthritis. But as far as specific organ sites are concerned, no, they weren't set up that way.

Baker: With the exception of, I guess, some cardiac physiology like the Surgery and Medicine Study Section or something.

Walter: Well, the Surgery and Medicine Study Section, I used to think that they would be more clinically oriented, but they're not. They're not clinically oriented at all. They're basic science surgical studies.

Baker: Well, this raises two very interesting philosophic questions. One is this idea of reviewing the grant proposals when they come in and making decisions on which Institute and study section they would be assigned to. Let me have your views on the effects of the decisions for assigning projects to study sections and Institutes and how that very important function, which isn't appreciated by a lot of people, affects the outcome.

Walter: Well, first of all, there are some study sections which would, just by their nature, have quite a lot of cancer relevance. For example--

Baker: Pathology.

Walter: No. Not Pathology. Radiation.

Baker: All right. Yes.

Walter: Now, there are some radiation proposals, even in diagnostic radiology, that would be cancer-related. But a lot of them in diagnostic would be more General Medical Science or maybe Arthritis even, or Heart Institute stuff, that would go to some other, like the Arthritis Institute. But in Radiation Biology they would almost always go to Cancer. Of course Radiation Therapy would just automatically go to Cancer. So, many radiation-oriented investigator-initiated grants would be assigned to the Radiation Study Section would come to Cancer.

Baker: But I'm focusing on the role of the DRG staff who review these and make these assignments. This is a function that affects the outcome which is not very well appreciated by even the grantees in my view, but yet it's a very critical decision-making step, because sometimes they look at the amount of money available in an institute, which affects which institute they assign it to, which is understandable.

Walter: The way DRG used to operate--I don't know how they operate now--there used to be Assignment Officers.

Baker: Yes. These are the people I'm talking about who make very key decisions.

Walter: And one of the Assignment Officers, whose name escapes me now, was the Executive Secretary of the Biochemistry Study Section.

Baker: Irv Fuhr?

Walter: No. There was another one.

Baker: I thought Irv Fuhr was Executive Secretary of Biochemistry for years.

Walter: There were two study sections involved in biochemistry. One was Biochemistry and another was called-- Irv Fuhr had the study section that had been created after the original Biochemistry Study Section.

Baker: Really? The other was I believe called Physiological Chemistry.

Walter: The Executive Secretary of this old established Biochemistry Study Section was also an Assignment Officer.

Baker: Don Larson was Executive Secretary of one at one time. But I thought it was the other way around: Fuhr for Biochemistry and Larson for Physiological Chemistry.

Walter: Larson.

Baker: He was in the Lab of Biochemistry when I came to NIH in 1949.

Walter: Larson. And he was also an Assignment Officer. He would take all of the grants of well-known people that were going to get funded, and they'd take them to the study section, and, since they couldn't give 100 priority to everybody, they'd try to get their priorities in order, and on the assignments, he took all the good people and gave Irv Fuhr what was left over. So he had a problem. When funds got to be tighter, this became a bigger problem.

Baker: I didn't know about this.

Walter: Yes. That was Don Larson. He would assign to his study section all of these people that he thought were really great, and they were, but the study section would have to give a range of priorities and some of them wouldn't get funded, and they should have.

Baker: Did you ever hear the joke about how you do this? You take all these grant proposals that have come in and you stand at the top of a long stairway and you throw them down the stairway and the ones that are higher up get the best priorities and the ones down at the bottom get the poorest priority. Have you ever heard of that joke?

Walter: I hadn't heard of that.

Baker: Well, it isn't really the way it's done. Irv Fuhr illustrated to me how an Executive Secretary in a scientific discipline can affect the course of research by discussing with the study section an area that needs more work in it in the view of the Executive Secretary. And the study section, if they agreed, would send word out that they were interested in having proposals in that area. And so Irv Fuhr demonstrated to me how, with grants, you can do a lot of things in influencing the course of the science. He was good at that. I think they had a significant effect even on training of biochemists.

Walter: You're talking about early days in the study sections.

Baker: Oh, yes. This is when I was with Ralph Meader.

Walter: And the Executive Secretaries did carry some weight in those days. Now, as time went on, the Executive Secretary became a guy that would just take notes and write up summary sheets, and he became less and less an important player in the activities of the study section, and the Chairman was really the main individual. The Executive Secretary would just sit there and take notes and the--

Baker: Well, even the good Executive Secretaries had to work very closely with the Chairmen, so it was a combination of a good Chairman and a good Executive Secretary that gave the best results.

Walter: Yes. That's right.

Baker: Which is not surprising.

Walter: But nowadays, I mean, they go and recruit Executive Secretaries, and maybe they'll be knowledgeable about the subject matter and maybe they won't be. You don't know.

Baker: Well, what accounts for this change?

Walter: I don't know what accounts for it, but there definitely has been a change. I think it's just a lack of qualified bodies.

Baker: Well, I think there are two reasons. One is that the workload of grant proposals has increased so much you do run out of top-flight people, both as Executive Secretaries and members of the study sections so that it's very difficult to keep the quality level the same time as you expand, particularly when it is very rapid. The workloads on members is also high and some are not willing to take on the task. And the other reason, I think, is that you're hiring a lot of people on bases other than their knowledge of the field.

Walter: Yes. I think that's true.

Baker: Including social engineering aspects.

Walter: True. But, I mean, DRG has a different mindset than Institutes, and I think that as far as the Cancer Institute is concerned, we were not able--the Grants Program--was not able to promote cancer activities until we were able to do our own reviews.

Baker: Well, not entirely. You could work with the Executive Secretaries sometimes.

Walter: But it was awful hard work.

Baker: Minuscule compared to the other.

Walter: For example, in starting out with program projects and centers, DRG said, "Well, we can do this review." But it didn't work out, because they have a different mindset. They'd get reviewers, different sets of reviewers, than we would get. And it wasn't that we'd get lesser qualified reviewers; we would just get different kinds of reviewers.

Baker: Yes. A point I was trying to make earlier. Yes.

Walter: And DRG was only too happy to get rid of the reviews anyhow. The Division of Research Grants' mindset is on individual investigator-initiated program project grants, period. Anything else, go ahead and take it. We don't want to deal with it, because you give us too much trouble. You say it isn't a good review and we're not doing right, and so just, you do it.

Baker: Well, it's just as well with the different mindset, I guess.

Walter: Yes.

Baker: Okay, here's a tough question. If you, as you look back, could have changed anything that went on, what would you have done, if you had that control and opportunity?

Walter: I don't know if--

Baker: Maybe nothing?

Walter: Well, I was just going to say that I don't think that we would have changed much of anything. I don't think that we, in the Grants Program, could have done much more than we did.

Baker: As Hugh Butt would say, you had a lot on your plate as it was. You did well to keep up with that, huh?

Walter: We were just happy to do what we were doing.

Baker: Yes. I think that's a fair statement. Another loaded question on whether you believe the developments in the Viruses Cancer field laid significant foundations for the development of molecular biology and, I might add, biotechnology?

Walter: I'm probably not a good person to answer that question.

Baker: Well, again, just impressions.

Walter: Yes. I think that's right. In molecular biology I tend to go beyond basic molecular biology. For example, in my early interest in cancer epidemiology, for example, for years, from an epidemiological standpoint, cervical cancer is a venereal disease. As time goes on, it seems to be more and more related to a *viral* epidemiological disease with papillomavirus and cervical cancer being very closely associated. But, from an epidemiological standpoint, aside from just the molecular biological aspects of it, there are other important aspects illustrated by such findings as very different incidences of cervical cancer and breast cancer in nuns.

Walter: Specifically on molecular biology, I don't know, but if you expand it to my general interest, what it used to be anyhow, I remember years ago if any of us would say, "Cervical cancer is a sexually transmitted disease," people would look at us as though we're nuts, we're crazy. But, because of the association of viruses in venereal warts and cervical cancer and so on, because of that association, I suppose you could say that's molecular biology. You can say nowadays that when we used to say cancer of the cervix is a venereal disease, nowadays you should say "sexually transmitted disease," it becomes more acceptable because of the Virus Cancer Program and that association.

Baker: But there was a dramatic shift with the findings of Temin and Baltimore on the reverse transcriptase and the work of Bishop and Varmus on oncogenes which partly grew out of Huebner's and Todaro's conceptualization of the oncogene with the information being transmitted vertically and not horizontally that changed the whole outlook of the cancer viruses area. It's no longer, for most tumors, that viruses are being transmitted; it's the coded information incorporated into the chromosomes that has the same kind of coding that you find in cancer causing viruses which led, in part, in the cancer field at least, to a shift from the focus on viruses to the focus on the genetic code information, and this is the change to molecular biology becoming the dominant and very rapidly moving field that it is today. And again, that development laying foundations for biotechnology. So, we really had a shift: like we had after Ludwig Gross's findings changing the outlook of viruses and cancer in that period, we've had another big shift again from looking at viruses to looking at the genetic code information. But the findings grew out of cancer virology where you first had to have the coded information in the viruses that produced cancer--what was it about those cancer causing viruses that made them produce tumors--and that gave you the specific coding for producing in cancers. But then Bishop and Varmus showed that you had that same coded information--very closely the same information--in the cell's own DNA. And this created, I think, another shift of outlook that was quite profound.

Walter: You see, you know a lot more about this area than I know, Carl. My knowledge of viruses and oncogenes and reverse transcriptase, and so on, are just kind of really superficial.

Baker: Well, you were in a different arena. Let me shift now to a broader philosophic question, and that's the perception of the public, the general public, about science in general, not even necessarily just biomedicine. But do you think the appreciation and understanding of science by the general public is better, the same, or worse now than it was in 1960? It's got to be impressions, of course.

Walter: Well, I think today there is a general mistrust of science, whether it be biological or the physical sciences.

Baker: Why do you think that is?

Walter: Well, there probably multiple reasons, and I wouldn't know how to rate them one, two, three, four, on down, in importance. But there has developed a general mistrust of science, especially in the physical sciences, relating to radiation and stuff like that. But, in the biological sciences I think people are getting fed up with people on television, every day they have to have some earthshaking medical news, and medicine doesn't advance day-by-day. I mean, there is not earthshaking medical news every day. But they have reporters that have to report, "Well, coffee is bad for you." "Oh, no, coffee is not bad for you," or "This is good," or, "This is not good," you know, and people go up and down, up and down, and one day this is good and the next day it's bad.

Baker: Do you lay any of the blame on some epidemiologists, or is it all the press' fault, or both?

Walter: Oh, I blame it on both. I think many-- But I wouldn't call them epidemiologists, because--

Baker: Well, they're reporting correlations, which doesn't necessarily mean cause and effect, of course.

Walter: You see, epidemiologists often report prevalence as though it's incidence, and there is a big difference between incidence and prevalence.

Baker: There sure is.

Walter: And incidence is a much more strict definition, but even that does not relate to causation.

Baker: Not always.

Walter: It relates to exposure to risk and exposure to risk doesn't tell you anything about causation. Just as I was saying about cancer of the cervix, you can talk about risk in nuns being much less than in the general population, but it doesn't tell you what the causation is.

Baker: It gives you a place where you might want to look though?

Walter: Yes.

Baker: Which is probably its main function.

Walter: But it doesn't pinpoint causation.

Baker: No.

Walter: But I think epidemiology is very important. Like when I did studies on leukemia and the geographic distribution of leukemia, the northern states were high and the southern states were low, in general. They are still-- We reported that blacks between the ages of 3 and 4 have a peak that is still unanswered. Why that, I don't know. It could be attributed to almost any number of things. But what it does, we really reported incidence and not prevalence, and that peak in blacks of incidence just reports risk but it doesn't tell you why and it doesn't tell you how.

Baker: How about educational institutions' role in teaching about science? Now I want to make a distinction between those who are going into science and those who are not.

Walter: Well, I think that those who are not going into science can get some exposure and learn something about the intricacies of science and perhaps get some feeling about the limitations that they should be aware of when they get reports of this, that, and the other thing. Unless you're really exposed to details in specific areas of science and know minute details about things, I mean, you don't really have an appreciation of the importance of very minute information. Like when I went through medical school, with doctors, they say it's an art and a science, but I think it's mainly an art because it's not much science. Physicians going through medical school get an exposure to various levels of science, but they don't have a real appreciation of specific scientific disciplines and many clinicians come out and talk about science and they don't know what they're talking about. I mean, they get the feeling that they are omnipotent about everything and they don't have the slightest, vaguest knowledge of what the heck is going on. And that's too bad, because many people think doctors know everything about everything, and they don't know anything about much of anything. They get a superficial exposure to various sciences and that's it. Very superficial. You see, I didn't even get an appreciation of mathematics and the science of epidemiology until I was at Johns Hopkins. And even there-- You see, when I went through Johns Hopkins and got my Master's degree in Public Health, I went there in a Venereal Disease Program, and we stayed there for 12 months, not 9 months. The academic year for most Master's in Public Health was an academic year of 9 months, but we had to spend a full year, and a good bit of that year was in the clinical side, in the medicine clinics at the hospital.

Baker: You had a statistics course though, I assume?

Walter: We had statistics, and it wasn't until I had that, that I was really able to appreciate some mathematics.

Baker: Did you have any math modeling?

Walter: Yes.

Baker: Oh, good.

Walter: Yes. We had math modeling and statistics. But again, I could only say it was superficial, because when I got into epidemiology and we were in the Biometry and Epidemiology Branch, and I was exposed to outstanding NCI biometricians.

Baker: That's a much deeper handling of the data.

Walter: Yes. And I would go to them and I'd say, "Hey--" I'm trying to do some stuff epidemiologically, and you had to do it mathematically--and they would tell me stuff and I'd just do what they'd tell me.

Baker: We had some very good people in that area. Jerry Cornfield.

Walter: We had some excellent people.

Baker: Marvin Schneiderman.

Walter: We had Cornfield, Schneiderman, and a guy named Mantel.

Baker: Yes. Nathan Mantel.

Walter: Yes. Mantel. And that guy was so bright. I would go to him and in 30 seconds he'd lose me. But whatever he said was all right. Nate Mantel. I mean, he was really something.

Baker: I was concerned that the people who are not going into science are not getting--I'm speaking of college level now--are not getting very good instruction about science, and I blame the science departments for this because they seem to be only interested, usually, in people who are going into science and they don't pay any attention to those who are not, and then they wonder why the public isn't more sympathetic to them.

And so, I've been teaching at Maryland, a course in general science, and I start with a bit about what science is and what it will do and won't do, and how you go about it, and cover physics and chemistry, evolution, genetics, even on into behavioral aspects and brain function, and weather and oceanography, all in one semester. So, I may have been loading it on too much, but I wanted them certainly not to feel negative towards science, but I thought they ought to have some appreciation of this much variety of science. I was not trying to make scientists out of them.

Walter: Well, yes. And I think that's good in a way because that enables those individuals to have some appreciation of the complexity and difficulties in science and be able to express some skepticism about a lot of the stuff that comes into the popular press.

Baker: Yes. In the first lecture I tried to get across the idea that science, which is both a process and a body of information and a body of knowledge, is never fixed and final. Any time evidence from experimentation or observation counteracts the theoretical interpretation, you have to change your interpretation, and that this, even though we talk about "laws" in science, they're not immutable and even Newton's laws, which lasted a long time and are still good for everyday life, had to be changed with Einstein's theory.

Walter: I know, in my own case, for example, when I went as an undergraduate student I had intended to be a physician. That was it. I was going to be a physician. And, as an undergraduate, what you could do, you could get a Bachelor of Science degree in Medicine. But I decided, "Oh, yes, you know, you get some embryology, and some zoology, and this, that, and the other thing; I'm going to major in a science." So, in high school I thought I was pretty good in chemistry, so I thought, "Well, I'm going to be a chemistry major." So I did. That was the biggest mistake I ever made, because I took courses with chemistry majors and I wasn't going to be a chemist, but they were, and I had to take, you know, quantitative, qualitative, physical chemistry and all this kind of stuff. And they were smart. And I was dumb. And I had all these lab courses, and I was a real klutz in the lab. And how I ever got through that stuff I don't know, but I got a degree in chemistry and I got in medical school for some reason. And then in medical school we'd have bacteriology. And you had bacteriologists in undergraduate school, and I realized what we were getting in bacteriology was just a superficial little bit of nothing. And we had biochemistry, and I realized too, this is not really as good as science faculty biochemistry. And we also had pharmacology, and our professor of pharmacology was not even an M.D. I say "not even." He was not an M.D. He was a Ph.D. But he knew a lot about pharmacology, and what he gave us was just superficial. And, as a result of the fact that I got a degree in chemistry, although I know nothing about chemistry and didn't even then, I was able to understand that what I was getting in medical school was not science, it was just kind of like jumping from wave to wave and getting a little superficial knowledge.

Baker: In a sense, I had almost the opposite experience when I came into the Public Health Service. You'll recall, in those days we had to take both a written and oral examination?

Walter: Oh, yes.

Baker: I was a graduate student at Berkeley in biochemistry, and so I was learning the basic in-depth biochemistry but, when I came in to take the exam for the PHS, all the biochemical questions were in clinical biochemistry, and I didn't know beans about the clinical biochemistry, but I knew a lot about the fundamental basic science of biochemistry. So, in a sense, I had almost the opposite experience that you had.

Walter: Yes. You see, we just kind of did superficial stuff, except in my undergraduate days in chemistry when I was exposed to people who knew something and I didn't, in medical school in science, *per se*, and even when I was at Hopkins. Later I was able to really appreciate how superficial it was and, looking back, realizing that people that really were interested in these disciplines really knew what was going on.

Baker: Yes. Well, I agree with your point. I did have a Physiology Professor who was excellent in the in-depth science and a friend of mine and I did a little bit of research activity with him. This was during the WW II, and he had a contract or grant--grant, I guess it was--to evaluate different sized molecules of gelatin as a possible blood plasma substitute. This was before we had solved the problems of plasma preparations. He also let us explore some areas on motility of the gut, kind of on our own, so that was sort of an introduction to some pretty good science in physiology, and the physiology course in medical school was the best course I think I ever had. It was also one of the most difficult courses. But, if you learned everything you should have learned about each experiment we did in the laboratory, you learned most of physiology. And it makes me very pained to think about how the animal rights people are beginning to block training and education where animals are absolutely essential. You're not going to be able to substitute computer simulation for that experience. I like to say, "Would you like your surgeon to be trained on a computer for his operations?" Can you make a comment about that area?

Walter: Well, my comment is that as long as I've been alive this antivivisectionist activity, as long as I've been alive, has been active. Maybe with PETA it's even more so than it used to be. But these battles have been raging for years and years and years and years and I guess they will continue. I don't have any knowledge as to whether it's more active these days than it was back in the '40s or not.

Baker: Well, how about the establishment of the Office of Alternative Medicine at NIH?

Walter: I think that's a bunch of bull. I think that's nonsense.

Baker: How did we get into that fix? Or how did NIH get into that fix?

Walter: Well, people are always looking for the easy way out, I think. It's always nice to think that there is something that's going to solve our problems simply. Some people always think that there is a conspiracy among doctors, or institutions, trying to keep something from them and that there is some easy economical way that you can cure this disease or that disease without going through all the rigmarole that you have to go through. And you get reports of--mainly anecdotal reports--about you stick a needle into somebody and it cures them, and this, that, and the other thing, and people want to believe that kind of stuff. So, what the heck. Let them do it.

Baker: But how did NIH end up with this, if you think it's nonsense?

Walter: Well, Congress made them do it.

Baker: Yes. This introduces an area that worries me about NIH, and that's the use of political decision-making dealing with scientific issues, which I think is a bad thing.

Walter: Yes. NIH has gotten away from what it used to be. It used to be a research organization. And I suppose some of the things that I, myself, did in the clinical centers, and so on and so forth, promoted it so that anytime something happens everybody says, "Well, let NIH do it. NIH should do this. NIH should do that." And you get into things that are other than what NIH was set up to do, and that was research.

I don't know why it happened, but I guess we just got so big that when a Government agency gets big enough, then people start doing things that are off the track.

Baker: You certainly get more political attention as the budgets get bigger, but the idea of micromanagement from not only Congress, but individual Congressmen, has increased in the last several years, it seems to me.

Walter: And then I remember when I was first in the Public Health Service, CDC was not looked upon as much of a research organization; it was mainly a service sort of a thing. But now it's gotten into being more of a research organization.

Baker: I don't object to that. Do you?

Walter: No. But it just shows how things change. And NIH was a research organization and it's getting to be more of a service organization. And CDC was a service organization getting into being a research organization.

Baker: Well, you know the old French saying, "The only constant thing is change."

Walter: Yes. But I think it's bad for NIH to start getting into service activities.

Baker: Well, this is why I really didn't want Cancer Control brought back into the NCI. I thought we had our hands full trying to develop the best research activities, and Cancer Control, to me, is not--most of it--is not research, it's a service function. Now, when we were required then to start it up again, I tried to put a flavor of research in Cancer Control, and there is some of that that is going on. A lot of their activities in that program are not just service, but are research. A lot of it is how you provide the service. There is still a research area to be had there. And then the one area that I think we've been very deficient in, in research matters, is the rehabilitation area for cancer patients who either are cured with deficits or those who are not cured but have real problems. I don't think our research in that area has been very good yet.

Walter: Probably not.

Baker: So, I was trying to make the point that if we had to have Cancer Control again, we should emphasize those areas where there was a shortage of control capabilities and hence special needs for more research, and it seemed to me that the rehabilitation area was a special one. I still think that's true.

Walter: Well, maybe so. Cancer Control has always been a big question mark as far as what kind of research you can do in Cancer Control. Dietary research, I suppose.

Baker: The physicists would call the data in this area of diet and cancer "soft data" or "non- rigorous data," which it is. It's correlations without an understanding of why or how.

Walter: Yes. The Centers Program used to be in the Extramural Program. Then when Tom King was Director of the Grants Division, Art Upton decided to put the whole Centers Program into Cancer Control, and it gradually deteriorated, because I think it got more and more into service functions than into research activities.

Baker: Yes. Now this is not necessarily wrong; it's just questionable whether it belongs at NIH or not. But, as you say, things have changed.

Walter: Yes. You see, my whole training and activities in the Venereal Disease Control Division, when I was in Florida, gave me experience in service operations. A lot of people don't realize it, but Florida, in those days anyhow, was really the leading state in venereal diseases in the country.

Baker: You mean in the handling of it, or in the infection rate?

Walter: In the incidence of it. We had high incidence of syphilis, gonorrhea, plus lymphopathia venereum, granuloma inguinale, and in addition we had endemic leprosy and--

Baker: TB?

Walter: We had TB.

Baker: And polio.

Walter: And a lot of polio. So we had a lot of activity going on. You see, when I first went down there, it was right after World War II, and there were some hospital ships that were left over from World War II, and so we had a neat idea. We were going to get a hospital ship and anchor it and put it in Jacksonville Harbor. Jacksonville had the St. John's River, and there was a big harbor.

Baker: A big harbor, yes.

Walter: And so we got this surplus hospital ship. Well, the first thing we found out, we had to have a Captain and three crew members, and we had to pay them, and they did nothing.

Baker: What was the name of that ship?

Walter: I forget the name of the ship. And the other thing was, it was hot in that ship. We didn't have any air conditioning in it. It was just plain hot. And, besides that, we tried to keep the males and the females separate for treatment, but we couldn't do it, and so we soon gave up that notion. So then we got the notion that there were a lot of surplus World War II airfields with buildings available, and so we got one in Melbourne, Florida. It was a Navy airfield that was surplus. And the government gave it to the State Board of Health for any use in educational or health matters. And so we took it, and we had an in-patient hospital where VD patients would come for treatment. And in those days, you know, we lost some syphilis patients from treatment with arsenic.

Baker: I administered the 5-day treatment for syphilis as a senior medical student. Yes. Mapharsen, an arsenic compound I.V. But the treatment only took 5 days instead of 2 years with the earlier treatment.

Walter: Well, usually it took 3 years. The continuous Mafarsen 5-day drip. We had that too.

Baker: I, fortunately, didn't lose any patients, but the student who ran the program, under guidance, before me lost one.

Walter: But that 5-day business didn't last long anyhow.

Baker: No. Because penicillin became available.

Walter: Yes. But we were still using penicillin plus arsenic compounds and we'd get so-called Herxheimer reactions and this that and the other thing. And then, you know, if you're using arsenic, you're going to lose a few people. And besides that, with neuro-syphilis we tried using these heat cabinets, and we lost a few people with those too.

Baker: With which?

Walter: With heat cabinets. We'd put a patient in the cabinet and heat them up.

Baker: Yes. Hyperthermia.

Walter: Yes, hyperthermia, for paresis, and also we were using tertian malaria. Now, that would be all right except for blacks, who were somehow immune to tertian malaria, and we'd have to try to use quartain malaria, which was not nearly as good, because they only got mediocre chills every fourth day instead of high chills every third day. But, in any event, we did away with in-patient care and then we developed out-patient clinics in Miami and West Palm Beach, Tallahassee, Jacksonville and Pensacola. And by that time, that's when I was able to get out of the VD business and get into NIH because of my interest in epidemiology. But then I went back. You know, I was a contract man for a while. I tried to develop a contract with the State of Florida for some leukemia studies that didn't work out.

Baker: Let me ask you about what we learned from attempts to control syphilis by treating it seriously as an epidemic. We didn't quite eliminate it like apparently we've licked smallpox, which I consider one of the greatest accomplishments of medicine. But we certainly reduced the incidence of syphilis drastically. What I'm getting at is what did we learn from that and, if any of that applicable in the AIDS situation?

Walter: Well, probably not.

Baker: First, how did we reduce the problem considerably?

Walter: Again, to get back personally. My interest in cancer was that cancer, in many respects, was like syphilis. It is. It affects almost every organ in the body, as does syphilis. And it was an interesting clinical phenomenon, both of them.

Baker: Both are. Remember what Osler said, "If you learn syphilis, you learn medicine as a whole."

Walter: I first got into venereal disease in Louisville, where we had a hospital, an in-patient hospital, and in those early days it didn't matter what clinical condition a patient had, if he had a positive blood test, that clinical condition was due to syphilis. He might have a brain tumor, he might have thyroid cancer, he might have almost anything, but if he had a positive blood test, we got him. And so we had agreements with the University of Louisville, at Louisville General Hospital.

Baker: What was this year?

Walter: This was 1946.

Baker: I had graduated two years before from there.

Walter: Or was it '47? It might have been '47. But, in any event we'd get all kinds of stuff, and then we'd get congenital syphilitics that had the typical saddle nose and the bowed tibias. But we were getting a lot of infectious syphilis and we'd have to do our dark fields and we'd get chancres and secondary syphilis and this, that and the other thing.

So, early on, syphilis was a very interesting disease, before the use of penicillin was widespread. You say, yes, syphilis is kind of endemic; it still goes on, while smallpox has been eradicated, I think it's the difference between prevention and cure, and there is a big difference.

Baker: There sure is.

Walter: People always talk about if they could only find a cure for this or a cure for that. I'd rather have a prevention of this, or a prevention of that. Why get cancer at all, if you can prevent it? Don't get it. You don't want a cure for it; you want a prevention. And we never did get a cure for smallpox; we got a prevention of smallpox. We have never gotten a prevention for syphilis. We have a cure for syphilis that's pretty damned good. But people still get syphilis, and you can treat it like a cold. But, again, syphilis, like smallpox, is, you get it once you're not going to get it again. Once you're immune to syphilis. You get smallpox once, you've had it, and you're not going to get it again. If you get syphilis once, you're not going to get it again.

Baker: I thought there were some exceptions to that.

Walter: No exceptions.

Baker: You know more about that, than I do.

Walter: Now, gonorrhea is still rampant, because you can treat gonorrhea but not prevent it. You can get gonorrhea today and I can treat you, and you can go out next week and get gonorrhea again, because there is no immunity to gonorrhea. There is immunity to syphilis, there is immunity to smallpox, there is immunity to measles, so the reason that syphilis is not eradicated is that we don't have a prevention. That's why.

Baker: I think we did a lot of good in reducing the incidence of syphilis by identifying those in the infectious state and making some reasonable efforts to segregate them.

Walter: Yes. But there is a lot of difference between, and there has been for many years, difference between syphilis and AIDS. Number one, we could interview a patient with infectious syphilis and say, "What are your contacts? Who are they?" and go out and get them.

Baker: That's what I'm getting at. That played a key role, I think, in reducing the incidence considerably.

Walter: Yes, that did. But we could offer them something. We could treat them. And that's the difference.

Baker: That's the biggest difference, I think, between them.

Walter: Now, with AIDS, people don't want to know because they can't get treated. There is no treatment for it. And, if you go out and you say, "Well, what are your sexual contacts," people cry, "Oh, you're interfering with my rights." You know, you can't do that.

Baker: That's probably why we have so many AIDS cases.

Walter: Some years ago I saw what they did in Cuba. They don't have this differentiation. If you're diagnosed with AIDS, they quarantine you. That's it.

Baker: Have they stopped the increase?

Walter: Yes.

Baker: Well, that was the point I was getting at. It seems like we've forgotten what we learned from syphilis.

Walter: But this call for or demand of individual freedom that is now in vogue interferes with successful handling of epidemics.

Baker: But this leads to irresponsibility of infecting others.

Walter: Oh, sure. But in Cuba, what they do, they just quarantine you and you go into this isolated area and that's it. And everybody says, "Well, look, they're infringing on those peoples' freedom." So, who gives a damn?

Baker: Well, earlier we used to quarantine people for a lot of infectious diseases and, sure enough, we were interfering with their rights, but it stopped the damned disease from spreading.

Walter: I know.

Baker: Well, I guess we're not going to be able to do that, for the reasons you've given.

Walter: I'm not so sure that, even if we did have a treatment for AIDS, this business of saying you're infringing on peoples' rights would preclude successful handling of AIDS

Baker: But, look at the facts. You get the spread and growth of the number of cases because we're not carrying out individual responsibilities toward others. And it seems like what we're looking for in everything is a balance between the individual rights and the population as a whole, and these are conflicting things, and the pendulum is now kind of far over on the individual rights' side of things.

Walter: At least now it is, in this country anyhow.

Baker: The last question is, do you have any other comments or questions you would like to bring up?

Walter: No. My only comment is I have an abysmal ignorance about anything involving viruses and cancer.

Baker: But you've given us some very good stuff from the historical standpoint, in addition to that area, which I think is important too, so I appreciate the time and effort you were willing to put into it.

Walter: I'm glad you came over. I'm glad to see you over here.

Baker: So, I think this was very important, even though you may feel you are not expert in that area. That's not the point. You gave us some very good information from the history standpoint. I think Victoria Harden will be pleased to get some of these thoughts about the grants area, even if they're not all in Viruses Cancer.

Walter: I hope so.

Baker: Very good. Thanks.