

SAMUEL HERMAN

This is an interview of Dr. Samuel "Bud" Herman, who was active in the NCI, in the Grants area, and in other roles at NIH, taken on May 1, 1995. The interviewer is Dr. Carl G. Baker, former Director of the National Cancer Institute.

Baker: Bud, I realize that some of these questions that you received ahead of time were designed more for those who were directly involved in the management of the Program in Viruses and Cancer, but I'm also interested in having some views from those who were not directly in the program and, as you know, I've interviewed 14 other people, including Bill Walter, who was also in the Grants area at NCI, and so we're interested in views from those outside the program.

Herman: Bill, as I recall it, had some involvement, at least to the extent with the Epstein-Barr virus, and he had actually done some African travel and was interested in Burkitt's lymphoma and nasopharyngeal cancer, so that he isn't entirely a virgin with respect to viral oncology, although he's been away from it for a good many years.

Baker: Before we get into the actual interview, could you give us a little bit of your background, of where you went to school and that sort of thing, and the experience that you've had? You've had a lot of different experiences, I know.

Herman: Yes. My undergraduate work was done at Harvard. I took my Bachelor's degree in 1940.

Baker: Major?

Herman: I majored in experimental psychology. And when I got out of Harvard, I had some military service and, as a result of my military service with the ASTP, I found myself at Loyola Dental School in Chicago and received a D.D.S. degree, in uniform, in 1944. And then I was in the Army for a spell, for a couple of years, and on release from the Army I enrolled in the graduate school at Yale in public health with a minor in microbiology, public health microbiology, and I took both a Master's degree and a Ph.D. at Yale in Public Health.

Baker: Who was your mentor?

Herman: Oh, I had-- He just died recently. It was a chap by the name of Bill Willard. He became the Dean and Vice President at Kentucky and built their medical center after he left Yale. He, for some reason or other, became a dominant figure in primary care, after that background. However, most of my contact in recent years that would have kept me current of what's

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happening in the viral oncology field has been small. I've done a lot of consulting for the L.P. Markey Charitable Trust, and it's almost like being a member of a study section. One of the big dividends is getting a chance to read applications which represent the thinking of, let's say, the most active, the brightest and best, before the stuff even gets published, when it's still an idea. I get to see requests to the Markey Charitable Trust coming from people like Leroy Hood and David Baltimore, and getting to see some of their thinking, and getting a chance to read, not only the proposal, but then subsequently reading their progress reports, because I'm responsible for abstracting their proposals and their progress reports. So, to the extent that I've kept up with anything in viral oncology, it would be by virtue of having read things involving Howard Temin and David Baltimore, and people like that.

Baker: Certainly Leroy Hood has been making progress in the analysis and synthesis of peptides and nucleic acid sequences made to order and the instrumentation that goes with it.

Herman: Well, he's made a business of it now. Of course, he's left CalTech, which is where he was when we gave him money, and he went up to the Pacific Northwest, I guess he's in Washington state--

Baker: The University of Washington.

Herman: The University of Washington. But he also has some commercial interests.

Baker: Well, that seems to be the trend these days, doesn't it? And when you were at NCI?

Herman: At NCI I worked for Ralph Meader and I was his deputy.

Baker: I guess that's when we first met?

Herman: That's when we first met, because NCI was good enough to allow the extramural people to attend the Scientific Directorate meetings on Thursday mornings, if I remember, and there I met people like Ray Bryan and Dick Rauscher, and so that whatever contact I had with tumor viruses came through that.

Baker: And you were there when?

Herman: I was there, I believe it was, around 1961 to 1963. It was in the early 1960s, obviously before Ralph went to Boston.

Baker: And you got some assignments in the radiation area?

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Herman: Well, yes. When I first came to NIH, which was 1959, I was recruited by a neighbor, Clint Powell, and I took over his position as Executive Secretary of the Radiation Study Section. I got to know a lot of people like Hyman Friedell, with many of the radiation therapists mostly, and a good many of the radiation biologists who had interests in cancer. So that's why radiation oncology was really more of a handle for me than biological carcinogenesis.

Baker: And when you left NCI?

Herman: When I left NCI, I went with Paul Kotin, and I became the founding Director for Extramural programs for that brand new--it was then called--Division of Environmental Health, which was subsequently transformed, if I can use that expression, into an Institute of Environment. And after that I became the founding Director of the National Eye Institute and, from there I entered a totally new career into academia. I went to Temple.

Baker: And you still have some links with Temple?

Herman: No, except for personal friendships. But I still have links in Philadelphia, in that they asked me, when I retired from my career at Temple, if I would be willing to start out and give them about 4-5 days a month at Jefferson Medical College. And that extended into an almost full-time thing. I've been doing that now since 1984, and find myself at Jefferson 3-4 times a month, and sometimes a couple of days at a time, and it's virtually full-time. I have to regulate it and say I really have other things, like my Markey work, and I do some consulting for the Southern Illinois University Medical School by virtue of a Temple friend who became the Chairman of Medicine there, Oliver Earle.

Baker: And your title at Temple was?

Herman: I was Associate Vice President for Research and Graduate Studies and then also Associate Dean for Research and Graduate Studies at the Medical School.

Baker: Well, you have had quite a mixture.

Herman: Yes.

Baker: Well, very good. That gives a good background, so we can start on the formal part of the interview with the first question, which really calls for an impression of, as you look back, of who some of the outstanding scientists were that were involved and what kind of key scientific steps come to mind as important steps in the development of the field. And I picked the date

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1950 to 1980 with the idea that in 1950 nobody thought viruses had any connection with cancer whatsoever and hardly any work was going on. Ray Bryan was one of the few who was keeping the flame alive, along with Joe Beard at Duke, and Burmester at Michigan State. Of course, Rous had produced chicken tumors with a virus way back, 1910 or so, but nobody believed him because the belief was that it couldn't be cancer because it was caused by a virus. So, there was a radical change in about 1955, along in there. So, being not directly in the field, do some key figures come to mind?

Herman: And the fact that if it would cause leukemia didn't make it exactly interesting--

Baker: Some pathologists said that leukemia was not real cancer.

Herman: Right. Well, I'm aware, not as an expert, but from having heard and read of lots of things that I can't associate names with. The one big thing, of course, that I associate names with, which everybody who reads good science writers these days would be aware of, are the names of Temin and Baltimore in the reverse transcriptase. And I take it that this was a really seminal discovery in this field.

Baker: Yes. I would call that the "second" revolution. The first one was to get out of this idea that viruses didn't have anything to do with cancer.

Herman: I agree. This is a good way to look at it.

Baker: I believe Ludwig Gross's demonstration of cell-free extracts producing leukemia, once the work was confirmed--and nobody believed him for a couple of years until they finally confirmed his work--that that created a drastic change and immediately we had other tumors, like Moloney leukemia, Moloney sarcoma--

Herman: Yes. I used to know him too.

Baker: Rauscher leukemia, Charlotte Friend and her tumor, which was a strange kind of erythropoiesis.

Herman: I would think that historically one would have to start with Rous and Shope, both Rockefeller people.

Baker: Yes. That's back in this very early period and then Wendell Stanley on some of the basic science.

Herman: Yes.

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Baker: And Sarah Stewart and her polyoma had considerable influence, I believe.

Herman: You said Moloney and Stewart. Now, these are names that I used to be very excited by.

Baker: Then another change that created a new outlook and really was the beginning, in part, of the shift from biochemistry to molecular biology. It came about the time of Temin and Baltimore's findings.

Herman: Well, I can mention things about which I would consider myself obviously not an expert or authority, but I would consider myself to be informed, and perhaps more informed than, say, a literate lay person. I was sort of in between. There are a number of things that I can't really associate names and places with, but they represent to me important building blocks, and I just wrote down a couple that occurred to me. Now, one was the idea, or the discovery, or the realization, of a human T cell leukemia lymphoma virus. Now, I don't know who did the really seminal work on that, but that was terribly important because it was something that wasn't endogenous in man; it was obviously something from the external environment. And the idea that it could possibly be an agent involved in AIDS gives it, you know an extra bit of importance. And that was really the only one of the RNA viruses. All the other viruses that I could talk about, or mention, like Epstein-Barr, would be DNA viruses. But this was an RNA virus. And then, speaking of AIDS, would be the human cytomegalovirus, which I guess is implicated in Kaposi's sarcoma. And one that I've run across an awful lot in my Markey papers would be the human papillomavirus. I guess that actually is known to cause warty tumors in humans, so there is no question about it. It's not just animal; it's in humans. And its possible relationship to cervical and uterine cancer.

And then I've put down here something about, obviously, the hepatitis B virus as linked with primary hepatocellular carcinoma.

Now, I have something that I put down here that I don't know how to formulate into-- Well, this was an event or a discovery. But this is the question of oncogenic viruses that derive their ability to cause--to bring about--say, malignant transformation from genetic sequences that we now, as a result of Huebner, call oncogenes.

Baker: Yes. Huebner and Todaro wrote a paper where, I think, the term "oncogenes" was first used. They didn't quite have it exactly right, but it stimulated, I think, an atmosphere of thinking about it, and then Bishop and Varmus actually found gene sequencing in chromosomes in which the sequences were very similar to those in cancer causing viruses. This led again to a shift of

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thinking from the external infectious agents idea to internal coded information which may or may not have originated way back from viruses, or vice versa.

Herman: Yes. But the whole idea that these were genes, some 20 to 30 of them, which are normally present in a cell but not of any concern because there is usually such a limited, or minimal, amount of expression and that somehow or other there is a relationship of an oncogenic virus to these sequences that are not necessary for normal viral propagation. So I don't know how you put that in words, but this was obviously an event of great importance.

Baker: Yes. And, as I say, I think it led to a shift of thinking about the causation of cancers from viruses to the genetic information which was either in the viruses or in the chromosomes.

Herman: It's kind of interesting in what I hope we're going to talk about later on, namely about directed research programs and grants and contracts. Well, I don't want to get into the balance between grant and contract research right now.

Baker: We'll get to that a little later.

Herman: Thus, the key figures are Varmus and Bishop, both coming out of the same Department of Microbiology at UCSF. Bishop, almost coming here to be the new NCI Director, but I guess he's excused himself. "Thanks, but no thanks." So that's what I would put down as being most significant. Most of these, I guess, would come under the rubric of biological carcinogenesis.

Baker: That's a good label, I guess. Yes. But molecular biological, I think, is the current way of looking at it.

Herman: There is a real question, I guess, whether cancer research has fructified molecular biology, or that molecular biology has really given great mode of force and thrust to cancer research, and I guess it doesn't really make any difference.

Baker: I think it's made a difference, because we've got a lot more scientists who are very good in the cancer field. And in the early days of cancer research, the belief was that it was scientifically a poor area to work in. It was even spoken of as a "scientific graveyard," if you were doing experimental work in cancer.

Herman: Yes. I remember that attitude. It's kind of hard to think back that that was the way people used to feel about it. And also an indicator of what you're saying is the fact that in the first talk that Varmus gave before a House Appropriations Subcommittee, describing himself as a basic

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researcher, he identified his work with cancer and he said, "Who would have thought, at the time we were doing the work that, you know, ultimately led to this Nobel Prize, that we were doing cancer research?"

Baker: Well, fine. I think that covers the first question. The second one shifts to the administrative people or management, if you wish, and who might come to mind as those who made some key decisions that affected the development of the field? First, let me pay tribute to those managing the day-to-day operations: in particular, Rauscher, Moloney and Stevenson were excellent scientists and superb program managers.

Herman: Well, at the risk of saying something inappropriate, I would obviously put you and Dr. Endicott in the pantheon of divinities that actually led the effort.

Baker: I've never been called that before.

Herman: Yes. You did lots of things, but you didn't do it specifically for viruses. You did it through your own views of science management, which included the work that you and Carrese did in the Convergence Technique, and Endicott's surrounding himself with people like you and setting up within the Cancer Institute major components of the Institute such as Etiology and Treatment Divisions, with these under separate directors in the Intramural Program. I would think that whatever relationship you and Endicott had to such things as the Special Virus Leukemia Program, which got started with \$10 million dollars, you saw the need to tie together various components into an integrated program. Now, I have a question here. At one point, in dim antiquity, there as a gentleman by the name of Harvey Scutter, and there was a Sally Myles, and they were involved in--

Baker: Who?

Herman: Sally Myles. Harvey Scutter: some grants money was earmarked to set up a program called the Special Virus Program for them to run. Do you remember what I'm talking about?

Baker: Yes. I can go back and give you some information. I got started into the Cancer Viruses aspects, from a program standpoint, when I was with Dr. Smadel in Building 1, and a lot of people in the polio game were really looking for something to do because the polio problem had more or less been solved, and so there were a lot of good virologists that were at a crossroads. So, there was a million dollars earmarked for cancer viruses work out of the regular NCI appropriation, and I remember calling a lot of these virologists who had been in the polio field, most of whom were

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friends of Smadel, and asking if they would be interested in putting in grant proposals for review, for NCI grants, and I also met with the V&R Study Section, and Scutter was the Executive Secretary of that.

Herman: That was the Virology and Rickettsiology Study Section?

Baker: Right. And they were meeting in Atlantic City. And I remember going to that. And I was proposing a plan for special integrated Program, and I showed a slide which, if you turned it at right angles, would look very much like a bare outline the Virus Leukemia plans we laid out later. And, of course, they would have nothing to do with the idea of planned research, but they agreed that they would expedite the review of these proposals so that the million dollars would be allocated and not not be used. And Scutter, who soon after moved to NCI with Ralph Meader, was the key figure in getting that NCI Program underway operationally. And that program grew some.

Herman: It did, because we used to joke in the--I don't know if we were still in the temporary building out on the reservation here--but we used to call it the "V Institute," because it was perceived growth potential, so at least for a short time it must have given evidence that it was about to take off.

Baker: Well, of course, the next step was the seeking of a special appropriation of \$10 million for the Special Virus Leukemia Program. Endicott, I believe, made the key decision to go after that, and Rauscher, Bryan, and I, with Zubrod also reviewing, put together a memorandum for Endicott to send to Shannon to request that Endicott be allowed to go and ask for this. And Shannon, as usual, to be very sure of the facts and the back-up for this, requested additional information. I remember, I was Acting Director, and a few days after the first memorandum, I signed a second one with additional information we had to send to Shannon. But then Shannon said okay, he would back it. And so Endicott asked for the \$10 million and then he came in to Carrese and me and said, "Okay, you guys have been talking about planning; plan me a \$10 million dollar program in virus leukemia."

Herman: I can picture how that happened because in a sort of miniature form, when the Heart Disease, Cancer and Stroke Program somehow came up, in those days, with a lot of money--it was about \$800,000 dollars--to be used for something called planning grants, and nobody said what they were, except the money had to be obligated by June 30th that year. That's all I knew.

Baker: Yes. Bill Walter got involved with all that.

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Herman: Well, first that was my program.

Baker: Did you get in too?

Herman: Endicott called me at home--

Baker: That's right. You had it first, and then Bill got it from you.

Herman: Yes, I had it. And Endicott called me, and he asked me if I would go to Providence for Congressman "Honest John" Fogarty, at the hospital that Calabresi was at, at that point, which was the old, I guess, Homeopathic Hospital, or something. It was not the Rhode Island Hospital. It was the other one, the lesser one. And I went up to Providence. That was my first site visit for this Program. I finally got all of that money obligated, but I know the picture. "Here's the money, now you get it spent by June 30."

Baker: And this wasn't just a bureaucrat trying to spend money; it was essentially orders from the Congress to get on the stick and get this thing underway.

Herman: Well, at any rate, so then I get lost. After the Special Virus Leukemia Program, I remember the leukemia and solid tumor efforts and the question, why not merge the two.

Baker: Well, we changed the name of the Program from the Special Virus Leukemia Program to the Special Virus Cancer Program, because we started getting viral-induced solid tumors as well as leukemia, and so it quickly became evident that the title should be changed.

Herman: So that towards the end of the '60s, what you were talking about was certainly a directed research program with the merging of those two.

Baker: Yes. '64 was when the Special Virus Leukemia Program was started.

Herman: Special Viruses. And in '68 was the merging.

Baker: That sounds right. Yes.

Herman: And, in between, was a Solid Tumor Virus Program, separate, because the pressure to merge Leukemia and Solid, there must have been something that bore the name of "Solid Tumor."

Baker: No, not in a formal organizational sense. Well, you see, one of the first solid tumors was Moloney sarcoma, and then polyoma was really solid tumor though it included leukemia. And

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Friend and Rauscher were very closely related to leukemia. But you began to have a whole series of solid tumors.

Herman: Oh, Charlotte Friend, that's another name I had forgotten about. And how about Melnick?

Baker: Yes. Well, Melnick was very active in the advisory apparatus for this whole development, particularly in the primate side.

Herman: And that was after he left Yale and went to Texas and--

Baker: Yes. Baylor. Yes.

Herman: Now you're recalling things for me that I've totally forgotten. But now, the second question is key administrative of management decisions, so those would be what I would consider getting you involved and having planned program operations. Of course there was Cancer Chemotherapy and Virology, but the whole concept, the operational mode, of the directed research programs, that I would consider to be the ground-breaking, pathfinding developments.

Baker: Well, you realize that not everybody thought that was a good idea.

Herman: Oh, no. I'm going to come, later on, to our friend Norton Zinder, because that I remember very well. I mean, Rockefeller, both as an institute and as a university, is deeply embedded in this early history of viruses.

Baker: I was surprised that people don't seem to make the distinction between research planning and research program planning. Program planning is at a higher hierarchical level than research planning, which is what you do in the lab. And a lot of people thought we were trying to tell people how to do their experiments, which we never were trying to do. As somebody said, "Can you imagine Sol Spiegelman letting you tell him how to do his research?" We didn't even think of that. I might as well say right now that the main reason for this was that some of these problems required an integration of different disciplines and skills and resources. How do you put all that together effectively? It was the need to tie together these elements into an integrated program that was the main reason for doing it.

Herman: In many ways, recent developments attest to the inherent wisdom and the value of the approaches that certainly I associate with you and Carrese, because I used to really hear about this and see it all the time. For example, when the DoD got its money, its windfall, for its support of breast cancer, it was interesting that an earmarked portion of that money went for

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what you were just talking about, for resources. One of your questions later on deals with that. But, you know, they have resources ranging all the way from tumor registries, to repositories, a lot of the things that you guys were talking about, that you had to think about and plan. I think people might be embarrassed if they remembered the stance that they had taken earlier in opposition to this.

Baker: Well, I don't know. I haven't seen too much of that.

Herman: I think that a lot of people that used to, you know, shudder at the idea, when Carrese would stand up there with a pointer and take them through, you know, a couple of hours, where they would really sweat and really resent a lot of the stuff, but in retrospect I think that you guys that are still alive could be extremely proud of the role that you played.

Baker: Well, I'm glad to hear you say that, of course. Okay. The third question deals with your participation and, as I say, much of that would be very interactive.

Herman: No. That would not be applicable. Now, four, "Who do you think were the main leaders who influenced the viruses cancer field?" Now, we mentioned a lot of them going back historically to--

Baker: I think the idea of this being a separate question from the first one is that the first one dealt with the active scientists, and they're not exactly the same people always, who provided leadership in a field.

Herman: Okay. Going back to the ones who provided--Well, Benno Schmidt, obviously. An enormously important guy.

Herman: Especially important was his co-chairing with Sydney Farber the Senate Panel of Consultants on the Conquest of Cancer. Mathilde Krim got involved.

Baker: She and Joe Burchinal put together most of the scientific side, which nobody paid any attention to. They went ahead politically and voted all this without much attention to the science.

Herman: So, I would consider names like that.

Baker: That's fine. I was thinking of earlier steps.

Herman: Earlier? Well, I also was thinking of, in a way, the part you-- Well, that would be Mary Lasker, I guess, in retrospect.

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Baker: Mary, definitely.

Herman: You simply have to her.

Baker: Sure. And Sidney Farber.

Herman: And Sidney Farber, and Senator Yarborough, and the--

Baker: Yes, leaders is what I had in mind, particularly in the next question, where I get into political figures, as well as the other people.

Herman: So those would be the names that influenced the direction. Of course, the very, very early ones, I don't know. It seems to me one time I had looked over a book that I'm sure I have downstairs by Mike Schimkin called *Contrary to Nature*, and that's a kind of an easy thing to do because, you know, the pictures and accompanying short articles are easy to review.

Baker: Most were based on the covers of *Cancer Research*. Mike introduced the picture covers when he was Editor of that journal.

Herman: And he tells you, you know, where they went to medical school and stuff.

Baker: Oh, it's delightful.

Herman: It's a delightful book to just flip the pages and see what Francisco Duran-Reynals used to look like as a young man.

Baker: Yes. I have that book. You might be interested in another personalized history of NCI that Mike wrote. What he said about me was that I didn't last long as Director because I thought I was the Director. That was very insightful, I think.

Herman: I can imagine Mike saying that.

Baker: I thought that was pretty good.

Herman: Yes. There were some pictures of people whose names I didn't even really know, but they were the more scientifically oriented. But I don't know any of the earlier ones before Benno Schmidt.

Baker: Well, I think, internally Ray Bryan was clearly a leader with the training and the philosophy for the younger people.

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Herman: And he was certainly along in years.

Baker: John Moloney was his technician originally.

Herman: And that was spelled M-O-L-O- Moloney. Not M-A, but M-O.

Baker: That's right.

Herman: And I recall Bryan as a guy along in years. When I used to attend the Scientific Directorate meetings he was already gray-haired and--

Baker: Well, as I say, he was the pioneer who kept the flame going when nobody else was interested.

Herman: Yes.

Baker: The sixth question deals with resources, and this includes not only the reagents that are used in virology, like antibody preparations and virus preparations, but tissue culture cell lines, animals, special animals, primates for example.

Herman: Well, my guess would be that certainly--and you tell me if I'm wrong here--but you had something called the DRFR, the Division of something, that Fred Stone was involved in at one point.

Baker: The Division of Research Facilities and Resources.

Herman: They used to give money out to get these resources going, and they would support people like, what was that group in Southern New Jersey, that was a-- Oh, cripes. I'm forgetting now. But it was a famous-- He had all kinds of animals in there but resources for cells. And, of course, nowadays, with the sequences in molecular biology, I don't know who it is that got it started, but the concept of having NIH fund resources that regionally or nationally would make sure that there was an equitable distribution to people that needed them. It wasn't just NCI, but DRFR, which is now the National Center for Research Resources. They had, along the way, they had a very important role in it would be my recollection. Why can't I think of that place in New Jersey, because it was a famous place?

Baker: Well, I think that came a little later, certainly in terms of magnitude and influence. You were talking about a later NIH Program. My question relates to the NCI Special Virus Leukemia and Cancer Programs. I would like you to think back about availability, or lack thereof, of these

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resources in 1964 compared with today, and I'm talking about quality controlled resources in quantity.

Herman: Well, one thing that I recall is that may be peripherally related, but related, is the idea that certainly in some forms of testing, which had to be done with accuracy and reliability, that there was always a question, particularly of an urban institution like, say, Sloan-Kettering, how much space in Manhattan they could allocate to, devote to, routine testing involving animals. And I guess the idea came that at some point these things came to be contracted out. Is this what you meant?

Baker: Well, Endicott started the philosophy of contracting which, in biomedical research, had not been done to any appreciable degree before the Chemotherapy Program. And he saw, as we did in the virus's area, that you needed to integrate a great variety of activities into one program if you're going to have a respectable drug development program. And so he said, "If I'm going to run this," which he was asked to do, "I need contracting authority because the freedom to allow individual investigators to go their own way in grants wouldn't work in a drug development program." So, I think Endicott started the idea of really using both resources contracting and sometimes research contracting because he needed to tie it all together. And this same philosophy we thought was necessary on the Viruses Program, and this is why we went in that direction. Also, I might tell you that those good virologists that came out of the polio field had a good habit of exchanging samples of reagents with each other to check out the purity and the quality and the claims for their research, and they were very good at testing this out even before they published. But I told them that, "By the time you send your samples around to all the other guys for testing, you don't have anything left to work with. You need quantities of this, and industry is the way to provide it." "Oh, industry can't make it good enough," was the academic scientists' viewpoint in those days. And I knew we were over the hump when Moloney came in one day, all excited, when he said, "We've got buckets full of Moloney virus from Pfizer and it's as good as anything we ever made. We've got buckets of it!" I knew then we were over that hump. And so now these things have been moved into commercial ventures and now we can buy all kinds of stuff that were not available then.

Herman: Yes. I wasn't close enough, but I know from a distance that these questions used to come up, but certainly this would be another example of management perceptions that Endicott and his entourage had that really advanced the field in so many ways.

Baker: I think so.

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Herman: Now, Question Number Seven is a very interesting question to me, because I remember--

Baker: This is the question that deals with the relative funding of grants and contracts.

Herman: I remember a paper by our late and great friend Dick Rauscher that appeared in *Science* some years ago in which, it seems to me, he was playing a great diplomatic political role to keep the so-called "outside" community happy. And at that point he had said he thought the ratio of the grants to the contracts supported in the field of virology was around 55:45. Now, does that strike a bell with you?

Baker: That's probably about right at that time. Yes.

Herman: And, of course, I don't know what it is now because it seems to me that one of the things that happened after the notorious, or the infamous, Zinder Report was that there was a tremendous opening up to the outside community because some of the objections in the Zinder Report were-- well, that was one of an early instance of raising a conflict of interest question. They didn't use that term, but they said that a lot of activities of the NCI staff were just extensions of the intramural people, and it didn't give a chance for some of the bright minds outside to get involved. And it seems to me there was a Monitoring Subcommittee of the Board that was set up under Harold Amos that was supposed to act on some of these criticisms. And the Zinder Committee had some criticisms in it, and I don't know what the merit of the criticisms were, such as the rigor of the scientific review that went on in some of these contract activities were questioned. You lived through that Zinder Report, I guess?

Baker: No. I'd already left.

Herman: You had?

Baker: Yes.

Herman: You remember when the Zinder Committee was brought in?

Baker: Oh, very much.

Herman: Who was the Director then?

Baker: Upton. But, Moloney describes the result of this as, "The demise of the Program." But it started a good while before the Zinder Committee met, and this was a shift which I think Benno Schmidt instituted, because he became convinced, after a while, by the academic scientists wanting the

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money moved into grants that the Program should be cut back or discontinued and certainly not allowed to expand at all. This was before the Zinder Committee held its first meeting. And Upton appears not to have been interested in much of anything but the grants philosophy; so, the program went downhill, so to speak, before the Zinder Committee met. The Zinder Committee Report was just the final blow.

Herman: The *coup de grâce*?

Baker: Yes. But now, what disturbed me about the Zinder Report was they didn't go into whether the science or the Program output was good or not; they were worried about Huebner having too much control, particularly Huebner, and they had a misunderstanding about the review of contracts. The peer review was probably more extensive with outstanding virologists from all over the country who were reviewing that program all the time and reviewing the contract proposals. But, since some of the academic people were not on it, they were not aware of this. So, one of the things we intend to do is to go back, if I can find the records--and I'm having a hard time--and find out who really was on these committees, because really outstanding people were on them.

Herman: Yes. I know what you're talking about because Jerry Green called me about a half year ago in response to some criticisms that had come up, and he wanted to know how the reviews were done, and I went through my "incunabula" downstairs to try to find things about, I think it was, the question of referral and assignment, and it's awfully difficult to put your hands on these things because in those days there was no Historical Office, the way there is now at NIH and FDA. They have their resident historians.

Baker: Well, they don't have enough. This one gal is about to work herself to death, Victoria Harden. She's doing a good job, but she has little budget and little space.

Herman: And we're talking about archives now, you know?

Baker: Well, it's very hard to find stuff.

Herman: And you have to strike while people are still alive and have all their marbles and can remember these things.

Baker: Well, I put in a formal contract proposal to NCI to support our travel to meet with a lot of people around the Country, and that was May a year ago and I haven't heard from them yet. In the

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meantime, Temin and Sabin, who were on our list beforehand, are gone. I wish I had gotten to interview them.

Herman: And then you would have-- You know, an interesting thing that I didn't mention before when Baltimore's name came up, where Baltimore and Temin were almost, you know, neck and neck in their work--

Baker: Well, they were.

Herman: --Baltimore's work was supported by the Allergy Institute.

Baker: He was also supported, particularly on resources, from the Special Virus Leukemia--the Cancer--Program. I don't think Temin was, but Baltimore was. Now, on this question of whether an individual scientist had too much backing, I think that's a question of how good the output was. You want to talk about a conversation with Phil Cohen at Wisconsin?

Herman: For some reason or other you had discussed with him the contrast between your experience at NCI when an idea, however egregious and important the idea was, had to be processed through the committees, but how it was more efficient and had far less paper at the Ludwig Institute and you did not have to work with so many committees.

Baker: With the Ludwig Institute it isn't as costly to either the organization nor the person who is seeking funding. As you know, now the thickness of just the instructions for both grants and contracts has gotten ridiculous. We used to be able to make contracts faster than grants. That's not so anymore.

Herman: Yes. With all of the certifications and assurances. Yes. Okay. So, at any rate, the business about if you could have changed anything in the viruses cancer field as it developed, what would you like to have changed and how?

Baker: That's a good question, isn't it?

Herman: Yes. Because, first of all, it's contaminated by the 20/20 hindsight, and so you can see things now-- But that's what you want to do. And what are some of your thoughts that might get my own thinking going on that?

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- Baker: Well, one of the persons I interviewed said we didn't stroke some of the people in the field sufficiently; that if we were to do over we should have paid a little more attention to that. It was an interesting way to put it. Stroke certain individuals.
- Herman: I remember, wasn't there some kind of rubbing? We mentioned Joe Melnick before. It seems to me that-- I don't know what was the impact of people who had their noses out of joint, and what would have happened if you could have gotten around that?
- Baker: I think it would not have been a whole lot different on the outcome. When we had the Airlie House meetings, which really were planning sessions in preparation for implementing the National Cancer Act, I was trying to build some *esprit d'corps* and get people together from different disciplines under some kind of structured rubric, which was the round target thing. You remember it? And I guess my impression was that about a third of the people were utterly opposed to planned research and they didn't want to have anything to do with it. A third thought, "Well, we'll go along and see how it comes out." And the other third said, "Well, it's about time you did this sort of thing." And I think that's probably generally true. And how much of this you do is, you know, debatable. If I had been Director a little longer, I think maybe I would have had some more meetings like those at Airlie House and maybe built better acceptance of this direction. And I was after building *esprit d'corps* because I was impressed in the early days of NASA, by God, those guys were going to make that deadline and they worked like it, and I was trying to get that same kind of spirit into cancer research, but that was one of my failures, I think. I also wanted input from outstanding scientists in an organized fashion, which the Airlie House meetings accomplished. This type of input directed toward the future rarely, if ever, comes from study sections, and from Councils (or Boards) is often inadequate.
- Herman: When you think of the contribution, say, of Varmus and Bishop, and when you think of what used to be the prevailing perception that many of us had, that the basic scientist wanted to be left alone and didn't want labels and identifications of this and that, I wonder, in retrospect now, were there many, many instances in which the involvement of the university community was really much more fruitful than one would have guessed? You know, when you say, "Gee, if we want to get things done, we really have to have a directed program, not directed research, but a directed program," and since that didn't become the dominant mode of operations, does it look, when you look back, does it appear that nevertheless important things happened, cascaded, and happened fast, so that maybe there was less to worry about by, you know, not having them having directed programs?

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Baker: It's hard to answer that. In World War II, yes. I don't think we can say absolutely, even today, that we necessarily made faster progress with the Program. I'm sure we did on the resources side. I think it's harder to say whether the research progress was speeded up very much from the employment of research contracts. I think so. But I'm quite sure the resources made a big difference. Also, let me reiterate, I am as big a backer as anybody on the grants system--and I was then--for exploratory research. You don't want central integration; you want probing in all directions. And so a lot of people, I think, thought because I was interested in planning that I didn't support the grant system. That's not true. Now, what proportion of funds should be in each category, that's very debatable. As part of review of our NCI plans in anticipation of passage of the National Cancer Act, I convened about eight of the top people, and we discussed that very issue. At the meeting was Lew Thomas, Ivan Bennet, Wendell Stanley, Sidney Farber, Harry Eagle, Harold Rusch, and Albert Sabin, and we debated the issue of how much should go to each area, and I finally got Harry Eagle to agree that some things ought to be done with planned programming, and then I said, "Well, Harry, I guess all we're arguing about is the amounts." But he didn't really want to admit that he had supported the idea. It's hard to say, even with hindsight. I'm quite sure that the resources made a big difference; their availability moved the field a lot faster. The research that was done under contract versus that supported by grants-- I'm not sure it makes much difference.

Herman: Uh-huh.

Baker: Application of the information makes a difference. Let me say that I think the Program did very well in the holding of the annual meetings of contractors, grant-supported investigators, staff and others. Those annual meetings got to be a highly valuable source of information where people really exchanged information ahead of publication time and developed collaborations. Gallo has continued this kind of operation where his annual meeting now is attended by hundreds of scientists. He was very much involved in the latter part of the program, and he was very impressed with the communication value of the Program.

Herman: Well, there are some little ways, I suppose, you could think of things that you do today that, if you had done those, it might have been even easier to do. For example, now the Director of NIH is given authority and dollars--they're shrinking now--of discretionary authority. If something really comes up that's hot, you have to trust to the judgment of the Director that this is a time to shift money into this, a small amount of money, and that really wasn't very common in those days. That might have been helpful for somebody like Endicott, for example.

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Baker: A Director can shift some funds. More important is budget development for the coming year. One reason I started using systems planning with the systems networking was for budget development. How do you decide how much budget you ask for in the different areas of cancer research of which there are great varieties? The systems network technique allows you to put things down and see their relationships, which are not so obvious sometimes, and you can sit there and think about what happens if I put more money here, or less money here, and you can see linkages that are important. And so originally that systems planning grew out of a need for a better basis for budget. It helped in making budget decisions. Also, we then fared better from NCI when we presented plans to the Council and to the Office of Management and Budget. The OMB staff would say, "Well, it's about time somebody from NIH told us what they were going to do with the money."

Herman: Well, didn't that go back to the PPBS (Programming, Planning, Budgeting System) and Wildafsky and--

Baker: Not exactly. Not exactly, because there was a big difference. I was NIH representative downtown during the PPBS mania that came from McNamara and his "Whiz Kids" in the Department of Defense when HEW had one of those guys from McNamara's shop (Alice Rivlin was Deputy to him), and they were busy trying to implement PPBS in DHEW. And you know that one of the tenets was that you ought to have good cost/benefit ratios. And I became a thorn in their side because I argued that you couldn't do that in research. And they kept pushing, and I kept pushing, and finally I said, "Well, let me give you an example. I can give you a wonderful cost/benefit ratio on breast cancer in women. If you take the breasts off at a very early age, you'll have a marvelous cost/benefit ratio, but I don't think you want to do that." And they said, "You're not very helpful." One of the things in the Convergence Technique is to show differences from the PPBS, which is too much numbers counting, and ignoring things that you can't count. And so we tried to show that you had to modify that philosophy for a research program. Your degrees of certainty are far lower and your time estimates much softer.

Herman: Yes. I'd forgotten all about that PPBS, and you were very active in that.

Baker: So, I didn't think it was quite right for a research organization like NIH.

Herman: My view of things is kind of superficial to say, well now, what could we have done that would have made the effort a lot more effective, more efficient.

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Baker: One thing I can think of is if I had stayed there and been able to have had some more meetings like we had at Airlie, I think that would have made planned programming more attractive and would have moved things along. I also was concerned that after I left the administrative detail got to where it was overwhelming the science, and I wouldn't have let that happen had I still been Director. And this was partly because we had a man with Carrese who was too good, too efficient. He worked night and day. And that was Jack McShulskis, and so in the big administrative volumes that were put together after Airlie the science content almost got lost under the administrative "trivia." Instead of focusing on the science the emphasis was on administrative detail, and that helped kill the Program.

Herman: Yes. Bill Gay used to love the term "administrivia." Well, I can't help you too much on that.

Baker: Sometimes my relationship with the Advisory Council (and certainly my one meeting with the Advisory Board) might have been better. Perhaps my expectations for the Council were too high and I let my disappointments show. The ninth question is sort of a loaded question, but do you think the Program laid the foundations for molecular biology and, I would say, biotechnology as well?

Herman: Well, I would say that certainly it's easy for me to imagine that a lot of what came out of that was a direct spur. Of course, people say that the biotechnology industry, as we know it, is an outgrowth of the recombinant DNA technology. To the extent that the accelerated progress in molecular biology is an outgrowth, or is attributable, to development of complex instrumentation, the development of new technologies, so what you're doing is that here is something that is a wherewithal of technology and an instrument which is actually stimulating growth and development of science.

Baker: Yes. This interplay between philosophic conceptualization and resources and instrumentation is an interesting subject, and I have the impression that there is not quite enough appreciation of the contributions made by the technology, the instrumentation developments, and the supplies of various resources.

Herman: Well, when you think of it, just take a field like microscopy and what's going on in microscopy today and now new techniques for using optical microscopes. You know, nowadays these people up at Carnegie-Mellon, what they're coming out with now in optical microscopy, there is no way that you could think of what's happening in science without being actually grateful for this tremendous development in instrumentation and in technology and techniques.

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Baker: It's all part of progress, and the pace has picked up dramatically. Look at the amount of data you can collect now compared to when we graduated from the professional schools. I used to count radioactivity samples one at a time. And you'd sit there, as a graduate student, studying while the stuff was being counted and then you'd take that sample out and put the next one in. Now, you know, you can run hundreds of them overnight with the data not only printed out but graphed for you.

Herman: Well, as a result of computerization, just think of the things you couldn't do then. For example, now, on these data banks, on the genetic data, sequences; that would not have been possible to do.

Baker: Yes. Wouldn't it be nice to be young enough to benefit from all these things?

Herman: I think of that all the time now as I get into Internet, that I wished to heck, you know, I'd gotten into this thing 10 years ago.

Baker: Well, I didn't get a clear answer to the question on do you think the program--

Herman: Well, I would think that a lot has happened. For example, what would have happened if you hadn't had all of this stupendous development going on and then you got hit with the HIV, with the AIDS epidemic? What a real head start. It doesn't seem as though that we've accomplished all that much, but just think where you would have been if you hadn't had concepts of retroviruses? And this was stuff that no one thought of. No one thought of an AIDS epidemic. And so now it's not unusual, as in an opening statement by Broder in those days, to be able to bring in a whole section on AIDS and retrovirology. All that became possible.

Baker: And we hope that's going to pay off. It hasn't quite yet.

Herman: So I would think it certainly was--to use the term--fructifying, that it actually rendered fruitful, developments in molecular biology. And, of course, molecular biology, if ever there was something, really depends on these sophisticated techniques and technologies.

Baker: And involving very special resources which now there is enough demand for them that they're commercially available. But they weren't in these earlier days.

Herman: You see now, for example, the work of Ventnor and Leroy Hood on automated sequencing--

Baker: Yes. I think this is marvelous.

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Herman: Unbelievable.

Baker: And Leroy Hood himself, he mixes both the conceptual aspects of biology and instrument development. It's a very interesting combination. So I'm a backer of Leroy Hood, even though I don't know him well.

Herman: And this guy, Venter, that left the Neurology Institute, that's out here in Gaithersburg somewhere, what they can do nowadays, they've cut down the time before you can do the whole human genome.

Baker: Oh, yes. Well, I figured that would happen.

Herman: And the cost.

Baker: Yes. Sure. Well, the tenth question really shifts gears a bit and is aimed at a much broader question than viruses and cancer. It's talking about science in general, and not even restricted to biomedical science, but science as a whole; and that deals with whether you think the perception and understanding of the public about science is better, worse, or the same as it was in 1960, say?

Herman: Well, in many ways, thinking about cancer, for example, it was a serious mistake then, and it's a serious mistake still, not to try to do something about the public's making naive assumptions. For example, "Well, look what we were able to do with poliovirus. Why can't we do this, you know, with cancer?"

Baker: Why can't we?

Herman: And then I get into something which I'm not sure how you'll react to it, but I really feel that there is an awful lot more--and it's so difficult politically to say this up on Capitol Hill--there is so much more that we need to know about basic biological mechanisms, how things happen, before you can begin talking about drug treatment or vaccines. By the way, we didn't mention that, and somewhere, in one of these questions, I would like to quickly add that one of the important things that I consider going on now that surely grows out of the things we've been talking about are efforts in the field of developing vaccines, and certainly we're seeing some of that with the hepatitis B, how you block replication of the hepatitis B virus. And so we mustn't forget that this could very well, one of these days, become an important thing and you could say, "Look, what we have now. We're on the threshold now of developing vaccines."

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- Baker: Well, we put--"we" the Program--put funds in Oak Ridge behind Norman Anderson to develop the centrifuge developments which are accounting for the fact that we can make decent vaccines now in ways we couldn't earlier.
- Herman: And there is a whole science of vaccinology now.
- Baker: I interviewed Norman Anderson last month.
- Herman: These people up at NYU now, Nussbaum, this is sort of a science in itself now, the science of vaccines, so we mustn't forget that. I think that, since ultimately what we're talking about is the public's money and how the public perceives the value and the importance of what's going on, there aren't enough periodic reminders that even though 10 years have gone by we're still playing the same record, we're still saying that we need to know this and we need to know that, and unfortunately that's true.
- Baker: Yes. Sometimes a broken record doesn't make it any less so, does it? However, I was also trying to get at the question of whether you think their knowledge of science and understanding of it is better, worse, or the same?
- Herman: Well, I think that there is more, to the extent that if you take the fact that, compared to, say, 15 years ago, that every Tuesday there is a voluminous section on science in *The New York Times*, that Mondays page 2 of *The Washington Post* can deal with anything from paleontology on down, that it's entered more into the common currency to think in scientific terms. Now, there still isn't what I would call a great deal of sophistication, but there is more of that now. On the other hand, there is an unbelievable amount of unsophistication up in Congress. For example, people like Congressman Arney, who is the number two man in the House of Representatives, who said something about, "Well, that isn't really Federal NIH research; that was done at Baylor." You know? And you say to yourself, "Well, Jesus, if people up on Capitol Hill are that uninformed, what does that mean?" And then I realized that somebody like this biophysicist, an M.D. biophysicist, a chairman up at Columbia P&S, Silverstein, who wrote a piece in one of the FASEB house organs about the importance of a grantee pointing out in interviews, in press releases, that but for the support from the Cancer Institute this could not have been done.
- Baker: Well, one thing that I didn't slip on was over-promising. I think DeVita did.
- Herman: Yes. This business came up with Murray Goldstein, who had been accused that in his dramatic style of testimony up on the Hill, that it was the old business of over-promising--"Now we've

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done this and we can look forward to--"and not enough caution to say that, "While this is a revolutionary, heretigmatic [?] change, it doesn't mean that next year we're going to have, you know, the--

Baker: Yes. I just always presented that there were opportunities that presented for additional research, and that's about as far as I would go. So, it's a fine line you have to walk, so that you make it sound like you ought to get more money, but you don't want to make it sound like, "If you give us this money, we'll have it by X date."

Herman: I'm running into now something that is very disturbing, and I'll even mention names to indicate that we have to take it seriously. Fink, up at Whitehead, the current Director of Whitehead, at MIT, who succeeded Baltimore, is one person, and our friend Manny Farber is a second person, who will laugh about this business of writing a grant application for multi-millions of dollars, and then you have your section in which you point out what the implications are for conquest of disease if you're able to really probe this totally un-understandable thing to ordinary people. And Farber says, you know, "Obviously we don't even think in those terms." He says, "This is what we want to do as scientists." This is the "hobby" research. Remember that term, the "hobby" research that Ken used to have. And I heard Fink say, at a Markey meeting where I was the rapporteur, and he made the point that he has a stock paragraph that he uses, or a page, that no matter what the application is, as he sends it into NIH, knowing that this is NIH, this is the paragraph that you never know--

Baker: Well, you remember the "all-purpose" pink sheet?

Herman: Yes. Or the computerized pink sheet in which you would have something on the budget you would have, "Modest." You were talking about over-promising; that's something obviously that has to be avoided. And then there are an awful lot of things that have to be done. We take a look now at the so-called "suggestive list" of what's going to happen when Kasich's Committee comes up with over the next 5 years they want to not only renew the cap on discretionary spending, but they also want to go down, to cut that down, so that there won't be more money to spend. And they had a person--I don't know if you know him--but his name was Mike Stevens, who is now the Minority Staff Director of the House Appropriations Subcommittee for HHS, and he was pointing out that it's the difference between "damaging" and "devastating." And he said that a lot of the sense of crisis that comes out of the funding prospects is driven by current success rates where one application out of four will get funded, and for the three people that don't get funded obviously this is a crisis. But, on the other hand, if there isn't going to be money,

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still, if you can manage to manage to maintain, maybe keep pace, with the inflation, the biomedical inflation, that this would be an enormous victory. This is really a "best-case" scenario, rather than one to grudgingly say, "Well, this is the best that we can do."

Baker: Well, with the national debt, something has to be done.

Herman: That if you're going to take seriously that by the year 2002 you're going to eliminate the deficit--

Baker: I don't believe it, but--

Herman: I don't think it can be done.

Baker: Well, it could be done, but I don't think it will be done.

Herman: Yes. I don't think that the people will--

Baker: We need to cut back somehow because that deficit is terrible. I mean, a lot of our money is just going for interest.

Herman: But see, if you see what is one scenario--I don't say a likely scenario--but if you take the Kasich scenario, he calls it a "suggested list." He says we take the fiscal '95 appropriation for NIH and we reduce it by 5 percent for '96 and then we keep it at that level until the year 2000. Well, this comes to about a \$2.5 billion dollar loss, if you take into account inflation and things like that, at a time when costs and expenses are going up. So, to say that this--

Baker: Well, \$2.5 billion dollars is not very much toward reducing the budget either, so this is the problem.

Herman: No. They talk about \$100 billion dollars like, gee, this is nothing.

Baker: Well, let me open another area, and this is the influx of political decision-making on scientific decisions. Do you perceive a change in that at NIH?

Herman: Yes I do. Oh, at NIH? Well, I was going to say I see it up on Capitol Hill, where you have a new--no more Chairman Brown, but you have this guy from Pennsylvania, what the hell is his name now?

Baker: I know who you mean.

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Herman: Walker. Congressman Walker, the new Chairman of the Science Committee. And, of course, NIH doesn't much care what he says because the only committees whose dollars depend on Walker would be NSF in the Science Committee, in their authorizations. But here is a lay person who is deciding not only on policy matters such as whether we want to put up legislation for a single Department of Science, excluding NIH but certainly having NASA and--

Baker: That's certainly a political decision.

Herman: It's a political decision. But, unfortunately, he goes beyond politics into science where he says, "Okay, now the Federal Government, our number one priority is going to be Federal funds have to go for just basic research; nothing that smells developmental or applied, like NIST. We're not interested in doing that." But then he turns around and says, "Except, let's say, for hydrogen research as an energy source," and, you know, the biggest producer of hydrogen is in his district up there. So, you have things like that, where decisions are being made of political dimension in a scientific field.

Baker: How do you like the Office of Alternative Medicine?

Herman: Well, it's-- You know, this was an interesting history. Jacobs, the first head of the Office--I just read an interview--is back in New Haven. I don't know what his connection to Yale is, but that's where he took his medical degree, and he's as much as saying that Senator Harkin from Iowa made life just totally unbearable.

Baker: As near as I can tell, the origin of this office is from pressure from a member of Congress, but my belief is, if Shannon were still Director, he would have not set up the Office.

Herman: You mean he wouldn't have gone along with it?

Baker: Right.

Herman: Yes. That's almost like saying that McNamara should have been a Shannon. He felt this strongly.

Baker: Well, yes. We should have fought the war seriously. And see, most of it is crying big tears because he was crying big tears. But my objection to McNamara is he didn't fight the war vigorously enough and so you killed a lot of people on both sides. Most people say, you know, we shouldn't have been there at all. Well, that's easier said than done.

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Herman: But, if you were in there, there is no substitute for victory.

Baker: Yes. But they didn't fight it that way. The Korean [War] was the same way. But I'm spoiled. I was in, as we say, the "real" war.

Herman: Yes. I agree that we're seeing a very troubling amount of this incursion into areas where a lay person-- Now, of course, we don't object when-- Well, you could say Congressman Brown is trained in physics, but, you know, most of the things he says we can live with and we like hearing him say that, but it's when a guy like Walker comes up now that you begin to see what are the implications of lay people making political decisions in science.

Baker: Well, I'm disturbed by that because I see a lot of examples. But I think it started a good while ago when we started requiring the filling of positions that really had little to do with biomedical research at NIH. So, I wouldn't have minded the position ceilings we had, if I could have had everybody working on cancer research, which we almost did in the very early days. Even the animal caretakers in the early days were out to try to solve cancer problems. I thought that spirit was wonderful. But it got fractured, shall we say. Well, I don't want to dwell on all that, but I am concerned that there is too much political decision-making and dipping down too far into the organization (micromanaging) by the Congress and political appointees in the Agencies. The interface between where the political decision-making is and where is the science is a complex subject. I think, for example, the total amount of money to be spent for cancer research is primarily a political decision, but how you divvy that up now becomes predominantly a scientific question.

Herman: This is the best way to articulate it because we get back to the old question--you remember Adam Wildavsky and the budgetary process—and...

Baker: Yes. Did you read that book?

Herman: Yes. Paperback. Yes.

Baker: I thought that was a great book.

Herman: And we always used to say that whether how much money goes into building bridges and schools, as opposed to supporting science that it's public money and these are--and they have to be--political decisions; that there is no calculus which tells you that this is the right number that goes in here and goes in there. But, having made that rough cut, that this is what you're going to

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be using to support biomedical research, you cannot have somebody up on Capitol Hill telling you, "Yes, but we want to have something go into muscular dystrophy."

Baker: Well, I don't know. As I say, that dividing line is not clear. I happen to think that the total amount in Cancer versus Neurological Diseases is a political decision, but I wish decisions below this level would not be made by politicians. One of the objections I had to the new Cancer Act was making the Head of NIH and the Head of NCI political appointments. I think that's a big mistake.

Herman: Yes. Yes.

Baker: Now, the Surgeon General? Right there on the dividing line.

Herman: Especially now. The Surgeon General is--

Baker: Well, of course, the position of Surgeon General I think, unfortunately, got destroyed essentially when you made the Assistant Secretary for Health position have all the authority that the Surgeon General had before.

Herman: And even before that, when you had Bill Stewart as Surgeon General and Shannon as Director, and Shannon made it very clear that maybe on paper it showed him as being under the Surgeon General-- Stewart used to laugh about that. He realized the realism of that situation.

Baker: Yes, but of course if we'd have had Surgeons General like Parran, the power would have been there probably. Well, we had an interesting time, didn't we?

Herman: Yes. Did Bill Walter say any provocative things?

Baker: Well, you know, he's kind of low-keyed, but he calmly made a lot of good points. Well, the last question gives you the chance to say anything else you'd like to say here on the record.

Herman: I don't know. The point that you just made about the political decisions, that's something that we mustn't forget, and I guess this is a very good way to end the discussion because, as you pointed out before, there is a difference between directed, as applied, to, you know, overall the level of program, as opposed to the research going on in the lab. This is an important distinction, and not to get frightened about efforts to systematize and rationalize how you use the resources you have in connection with the problem you're setting out to solve. I think that is a big contribution that you guys made.

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- Baker: But you see, there are people that say--and I remember Henry Kaplan often said--that if you did your study section review well and your Council review well, all these other problems would take care of themselves. I don't believe that, but he did.
- Herman: Ralph used to say that.
- Baker: Oh yes, Ralph Meader.
- Herman: Ralph used to say that there was no point of identifying priorities; that they automatically, and without error, got identified through the decisions of the thousands of individual scientists writing proposals, reviewed by the study sections and--
- Baker: This is why, when I became Director, I quickly reviewed the distribution of funds in different aspects of cancer. For example, I checked on the number of large bowel cancer grants we had. We had nine of them, totaling only \$212,000. Yet, if you put male/female statistics together, large bowel cancer is the largest category of cancer. And here we had a mere \$212,000 effort. That is an example of why the grants system may not always work. And that's why I set up the Organ Site Program. Then we began to have more work on large bowel cancer. A similar picture was found with cancers of the prostate and urinary bladder. Yes. But, as again I'll reiterate, I still would back the grant system for a lot of the effort. So it's not "either/or," you need both kinds of things it seems to me.
- Herman: But the one thing, and I don't know how you can make this publicly appealing enough so that it doesn't cripple you, and that is that much as things look like we're really on our way, that we don't really have enough understanding of things like, say, the life of a virus, the life history of a virus--having important understandings of that type--before you can begin doing drug discovery for the treatment of AIDS.
- Baker: Well, let me ask you a question that's along those lines. We've spent tremendous amounts of money, we've had some of the best thinkers in history putting a lot of effort on trying to do something about cancer and ideally eliminate the whole thing. Why aren't we further along?
- Herman: Uh-huh. Well, one answer, I suppose, could be the intractable nature of the problem; that it's like an infinite onion. You keep peeling off layers and you don't get to the bottom of it.
- Baker: Well, basically I agree. My answer is *complexity* of living organisms.
- Herman: Yes. Well, we're saying the same thing there.

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- Baker: I think so. And somehow we keep trying to simplify things. And I just read the other day where Senator Moynihan from New York has said, "We're going to have to learn how to deal with complexity. We can't keep on simplifying, because it's not simple." And I think that's true in the organism. It's not simple. And we haven't learned how to handle complexity very well.
- Herman: Well, one thing that makes me feel good is the status today of structural biology and consequences like rational drug design. It is no longer as hit or miss where, as Philippe Shubik, a member of the Council, used to say about cancer chemotherapy, "You take a bottle off the shelf, you put a little in here, and a little of that, and you try it out on the patient," and Sydney Farber would be exploding. "Shubik," he says, "I wish you would withdraw that statement." But what we're saying is that rational drug design can only come from a knowledge of intermediate pathways, knowledge of protein structure, and the most basic kind of biochemistry.
- Baker: We're beginning to get a hold of that now, I think. And computers are helping tremendously.
- Herman: Now you know where in the molecules you are blocking activities.
- Baker: And the computerized simulations where you can visualize the interactions of the molecules and turn them in 3-dimensional graphics, and you can see little depressions, and you make a drug that fits into that depression.
- Herman: Computer graphics aiding rational drug design.
- Baker: This, I think, is a radical step forward.
- Herman: I find that to be the most comforting thought.
- Baker: That's one of the best advances, I think. Yes.
- Herman: So, if we could have more of that. But you call it "complexity," and I say it's just the intractable nature of the problems we're trying to solve.
- Baker: Well, I refuse to think that it's intractable.
- Herman: So, it's good to end an interview on a note of agreement like that.
- Baker: Well, you and I don't disagree on very many things.

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- Herman: And I like your thought about, from your background, coming out of a place like Berkeley, that it would be unthinkable that you didn't have some feeling for the Grants Program as opposed, say, to the Contracts Program. It would be unimaginable.
- Baker: Yes. It takes both approaches, it seems to me, and then you can always argue about the relative amounts, but other factors get into that decision.
- Herman: And you get politics into that too because politically it's more important for somebody to have more money getting more people happy, which is what you do with the Grants Program, more than you do with programs funded with contracts.
- Baker: Of course, I wasn't out to make people happy. I was trying to get people to try to move towards solving problems in cancer.
- Herman: You know, it isn't just education of the public, but education of the--if you talk to Tom Kennedy--education of scientists. A lot of the people who really ought to be disturbed about what could be happening at NIH in the Intramural Program and the Clinical Center, I've run into this in Philadelphia, so maybe I'm--
- Baker: Well, it's an age-old problem.
- Herman: It's the business of these scientists who think, "Well, it means more money for us out here in grants." But not necessarily. It isn't. It ain't going to happen. If they cut down, if they down-size--what they call REGO-II--they reinvent themselves to a point of inefficiency out here, it isn't going to be that the dollars that you save are going to be used so the success rate is better.
- Baker: I don't write to Congressmen very often, but I did write to Connie Morella and Sarbanes and Mikulski about Tom Kennedy's write-up.
- Herman: He had a nice session with Morella and her legislative--
- Baker: I got a nice letter back from Mikulski yesterday and from Sarbanes last week, and I haven't heard from Morella yet. I don't know what good that does, because those three people are pretty strong supporters of NIH anyway.
- Herman: This is the problem I have with the--
- Baker: But Senator Mikulski said she could use some of these arguments, and she was writing to Shalala.

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- Herman: She's the Chairperson of the Technology Subcommittee of the Science Committee, which puts her in a very, very funny spot, because if they gut the NIST program, that's one of her constituents, and that's what Walker says, that they're going to really cut the ---- out of that program.
- Baker: Cut the "what" out of the program?
- Herman: And also, you know, you have to keep in mind that, as a Republican, if Connie Morella gets too sympathetic to Tom Kennedy's views, that they can begin denying her things like chairmanships.
- Baker: Well, that's all part of the game.
- Herman: What I do is, I write to these people when the retired officers tell me, you know, about HCFA subvention of DOD health care, which means that when we go to the Navy that they get paid for what they do for us through Medicare. Now, I wrote-- I got a very nice letter from Mikulski, who not only assured me that she goes along with that, but she's a co-sponsor of the legislation that hasn't yet been introduced in the Senate, but already exists in the House, which would authorize subvention, which would give the incentive to the Commander here at the Navy to get the resources to take care of the over 65s.
- Baker: Of course they're going to be cutting back Medicare payments too.
- Herman: Yes. They'll be cutting back on that. But it seems to me that that would be, for people like us who are considered to be the ones that could afford it, that we shouldn't be, you know, getting that. But we would be lost with the retirees that could be handled there, and in fact I think that would even be better.
- Baker: Well, we'll see. It's interesting times, as always.
- Herman: And so, we'll see with the next election.
- Baker: I appreciate your--
- Herman: And I thank you for this because I have to get some batteries for my other machines, and I want to try that out.
- Baker: I appreciate your time and effort.
- Herman: I can see now why you said it couldn't be done by telephone.

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Baker: No. Not nearly as good. Well, thanks very much, and I look forward to seeing you shortly.

Herman: And you have a good game of golf.

Whereupon, the interview concludes