NCI ORAL HISTORY PROJECT

INTERVIEW WITH

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July 9, 1997

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National Cancer Institute Oral History Project
Interview with Carl G. Baker, M.D.
conducted on July 9, 1997, by Gretchen A. Case
at the offices of History Associates Incorporated, Rockville, Maryland

GC: This is Gretchen Case talking to Dr. Baker. We're at the History Associates office in Rockville, Maryland. Today is Wednesday, July 9, 1997. It's about 10:30 a.m.

We've talked once already, and I told you that I wanted to bring you back for another interview, just to kind of fill in some blanks. And you were saying something interesting just before I turned on the tape about the perception that history at the NCI started with the National Cancer Act. Could you tell me a little bit about what we were talking about just a minute ago?

CB: Yes. I commented generally that it seems that many people are actually ignorant about history, or they are not interested in it. Often they visualize what happened only in terms of what started when they appeared on the scene. I find it a bit surprising that so many people aren't interested in history, but tell the story as though it just started with their participation.

For example, the Chemotherapy Program actually started in 1953 with Dr. Endicott being asked to head it up. But Dr. Zubrod, heading it later, told the story almost as though it started when he was heading the program, although he was certainly aware of and often did mention Dr. Endicott's contributions. But so many people think it started at that point. More recently others think it started with the signing of the National Cancer Act.

The other point I was making was that definitive results of research, particularly in clinical investigations, often are not available until many years have passed since the research efforts actually started. This is particularly true in evaluating drugs clinically in cancer. In carcinogenesis research, you may have two decades before the results are actually in hand.

So a lot of programs were started much earlier than the National Cancer Act, but the results didn't show up until the Act had already been signed, often for some period of time.

GC: So it was credited to the National Cancer Act, even though the work was—

CB: Well, a lot of people think that most of these things were started because of the new Act, my point being that many of them were started well before that, and particularly a lot of the planning for a new National Cancer Program that resulted from the Act was done also before the Act was signed.

GC: Right. And we talked about a lot of that last time.

CB: Yes.

GC: You gave the example of Dr. Endicott working on the Chemotherapy Program before Dr. Zubrod arrived.

CB: Yes.

GC: Were you working with Dr. Endicott on that program?

CB: Not at that point in time. I was an Assistant Director with Dr. Heller, and Dr. Endicott and Dr. Sessoms were running the NCI Chemotherapy Program physically in the building in Silver Spring, rather than on the NIH campus.

GC: Do you know much about those early years before Dr. Zubrod arrived?

CB: Yes. Actually, I think nobody at NIH was interested in having that kind of applied program, as some people see it, a search for drugs that were capable of treating cancer patients. And the Congress actually ordered the NCI to create such a program.

Dr. Endicott before that was Scientific Director of the Division of Research and Grants, and doing a good job; so he was asked to head up this new Chemotherapy Program. He realized that to have a drug development program required integration of one part of a program with another part, namely the animal screening for anti-tumor activities had to be tied in then with work on the pharmacology and toxicology of these selected agents, first in animals, and then cautiously introducing in Phase I chemotherapy trials the initial testing in human subjects.

The Phase I trial was simply to find out where the toxicity levels were. If those drug candidates that looked like they were safe enough to use at the doses involved, then, partly based on the animal data, Phase II trials were instituted to find out if there were anti-tumor effects at the acceptable dosages. If that proved positive, those compounds were selected for

Phase III trials where larger numbers of subjects could provide requisite statistical aspects of the data.

Dr. Endicott realized that the philosophy for grants, which gave a great deal of leeway on what the grantees could do, would not allow an integrated program for carrying out projects ranging from the acquisition of materials and testing in animals on through the Phase III clinical trials, all of which required integration of program segments. And this meant also that he thought he needed authority for contracts where more control from the government could be imposed, if necessary, to make sure that the contractors were not free to go their own way as was pretty much the case in grants.

This was the initiation at NIH of the use of research contracts. And Dr. Endicott of course was later then made Director of the NCI.

GC: Right. Okay. Also, I'd like to talk to you about the early years when you were there. We talked about some of the positions you held, but, for example in the Laboratory of Biochemistry when you first came to the NCI, can you tell me a little bit about the kind of research you were doing there and who you worked with and what was going on at the time?

CB: Yes. I had been taking biochemistry at the University of California at Berkeley in 1947 and 1948. In 1948, Dr. Jesse Greenstein, the head of the Laboratory of Biochemistry at the NCI, gave a series of lectures at Berkeley on the biochemistry of cancer, and these were wonderful lectures. He gave all of the lectures without any notes with the exception of when he had to put data on his blackboard.

And he had written the first excellent book on biochemistry of cancer . . . that was worthwhile. There was an earlier book, but it was very confusing.

Anyway, these were wonderful lectures, and after the lectures, we'd have a lot of discussions about cancer and biochemistry. So he offered me a position in the NCI Laboratory of Biochemistry, and I began there on January 1, 1949.

It was very impressive. I walked out to the NIH from downtown Bethesda on New Year's Day, and went to Building 6, which at that time was all most of the NCI laboratory activities. Dr. Jay White was already there feeding his animals. Dr. Al Meister, who later became my section head, came in and started work. Then Dr. Greenstein himself came in. So here on New Year's Day, I got a real introduction to the staff hard at work on a holiday. I thought that was rather impressive.

But it was not unusual. The Laboratory of Biochemistry staff was used to working two or three nights a week, plus weekends. And a lot of this was Greenstein's motivation and inspiration, if you will. He was an excellent laboratory man, so he was a wonderful mentor for teaching you some of the finer details of laboratory operations.

The first scientific paper I wrote resulted from the work at Berkeley, and it was on the study of cholesterol in tumor-bearing mice and rats. Little—in those days, hardly anything—was known about cholesterol metabolism and cancer, so I thought it would be interesting to find out a little bit about that area. By giving radioactively labeled acetate to animals, you could find that the radioactive carbon atom ended up in cholesterol.

This initial probe was to see if there was any difference between the tissues in the tumor-bearing animals compared to the non-tumor-bearing control animals. Also what about the tumor tissue itself? It was an interesting introductory probe.

The next two papers were also on cancer in tumor-bearing animals. In one case, tumors were produced by feeding butter yellow, a potent cancer-causing chemical. In another case, we had animals that had a high incidence of tumors. So there I was looking at fatty-acid metabolism.

But after those two papers, I fell into the same mold as the rest of the laboratory in terms of emphasis on the resolution of optically active amino acids, the building blocks of proteins. Amino acids come in two forms. One is called L amino acids, standing for levo, which means to the left, and the other is D for dextro, meaning to the right. This goes back to Louis Pasteur, who first found out about this optical isomerism where certain kinds of compounds come in two forms.

When one synthesizes amino acids in the laboratory, you'll have approximately a fifty-fifty mixture of D and L forms. The reason we say left and right is that when you make solutions of these materials, the D forms rotate polarized light to the right and the L forms rotate the polarized light to the left.

GC: Oh, really?

CB: You can measure this very accurately with instruments. And Pasteur first noticed that crystals of tartaric acid, potassium tartrate, physically were mirror images in two forms. He could pick out with tweezers crystals in the two types. When he put those in solution and looked at the polarized light, he found that they could rotate equal and opposite directions if you put the same amount of the D and the L forms in the solution. And he could correlate then the optical activity with the actual physical structure of the crystals. They were mirror images of each other.

And in our bodies, we have only the L form of amino acids. In most of nature, in the biological systems, you'll only find the L form. (Now, there are certain bacteria where you'll find D forms, but they're exceptions.)

Why we're that way is not clear, but there has been a lot of speculation that it's more efficient to have only one form, and the enzymes are very critically related to this optical isomerism. So it's probably more efficient; it evolved that we only have the L forms.

Well, anyway, Greenstein and his group had discovered an enzyme in kidney that would act differentially, so if you made certain derivatives of the D and L amino acids and subjected those mixtures to the enzymes in kidney, the kidney enzyme would act only on the L derivative and not on the D derivative. And then you could separate the two on the basis of physical properties and split the side group off that D form with acid, and you'd end up with pure form in good yield; in one hand the L form, in the other hand the D form.

This was very important in those days because commercially you'd buy a lot of amino acids, and they would be labeled D or L, but they often were not. They were often mixtures. And a

lot of bacteriology and nutrition work got clarified by the availability then of pure D and L forms. So this was commercially developed by several companies, and the enzyme was very easy to make. You could grind up hog kidneys. You didn't even have to purify the enzyme to make it work.

So we explored then this process in all the natural amino acids first, and what I did was see if unnatural amino acids, namely those that chemists synthesized that were not available in biological systems naturally. I was able to extend and show that it worked at higher, longer chains of amino acids than those normally found, but there was a limit. With Herb Sober we used chromatography with the Greenstein procedure to obtain both isomers of various amino acids applied to very small amounts and to obtain both isomers of isovaline, a very soluble compound.

Then I converted those amino acids into alpha-hydroxy acids, which are also optically active with L and D forms, and did some studies on their properties and metabolism.

I think the best paper I was on was with Greenstein, Leon Levintow, and Jay White, on the four isomers of isoleucine. This amino acid has two optically active centers, so instead of just D and L, you get D, L, and allo-D and allo-L. So there are four isomers, and we were able to separate all four of those using the same principles that Greenstein had discovered.

And here we actually did feeding experiments on young mice and showed that only the L form supported growth. The other three forms would not. So this, I thought, was a very nice paper.

Incidentally, Dr. Levintow later became head of Biochemistry at San Francisco, University of California.

Now, after Greenstein saw that I was willing to work some at night and weekends, he made a reorganization in which he appointed Alton Meister a section head, and I was put in his section. And Al was a very good program leader, too, and another hard worker, and wrote many papers. He was on the editorial board of the *Journal of Biological Chemistry* for many years. He recently died. He was head of Biochemistry at Cornell, which was a job he particularly was glad to have because previously Vincent duVigneaud, a Nobel Prize winner, was sort of a icon for Al Meister. DuVigneaud got his award for working out the structure of oxytocin, which is a pituitary gland hormone that is used in obstetrics—after delivery of a baby, you inject the oxytocin, it makes the uterus contract so you have a lot less hemorrhage.

And the compound oxytocin was an interesting circular compound, where eight amino acids (L forms only) were joined together to form a ring. DuVigneaud worked all that out.

Incidentally, duVigneaud was invited to speak at the Lab of Biochemistry, as were many other very famous people in biochemistry. It was another joy as a young person to be able to meet and talk with these outstanding biochemists that Greenstein knew and invited to come and talk.

And he would usually have a little party at his house in the evening, and we would have fun informally with these people. One of the Danish greats in those days was Lindroström-Lang—he played the piano and sang songs. And Hans Neurath—most of

his career was at Duke—had a whole array of jokes, as did Levintow, and they would tell jokes back and forth all evening. So we had a lot of fun with that. It was important too.

Others in the Lab were Vince Price who worked closely with Greenstein for years; and Sanford Bierenbaum; Paul Fordor from Israel. Greenstein invited foreign scientists to work at his lab, so we had a lot of people from various countries that worked in the lab. It was a very dynamic and inspiring place to work, and high quality was topmost in everybody's minds.

I think I told the story about questioning one of Greenstein's melting points?

GC: No. You didn't tell that story.

CB: Oh. Well, Greenstein, as I said, was an excellent laboratory scientist—in his techniques and all. And in work for this paper on the isoleucine I had made some derivatives and done melting points. I got one melting point that was different from what Greenstein had already reported in the literature.

I remember recrystallizing this material four times and drying it thoroughly before I took the melting points, and I kept getting this different melting point reading. So I finally screwed up my courage and went in and told Greenstein I thought his melting point was incorrect. You could see the blood sort of rise in his neck up to his face—

[Laughter]

CB:—but he did the right thing, of course. He said, "Well, let's get the melting point apparatus." Fortunately, I was right.

GC: Oh, you were right.

CB: Yes. But he was excellent with laboratory techniques, so you learned a lot from him. So that was another little sidelight.

GC: Was he hard to approach? You said you had to screw up your courage.

CB: No, no. But you knew he had a bit of a temper.

GC: Oh, really?

CB: He unfortunately died of very high blood pressure. He was a little overweight. He didn't smoke cigarettes, but he smoked cigars and pipes. In fact, all of us smoked cigars in those days in that Lab partly because Greenstein and Meister both were cigar smokers. When my first daughter was born, I started smoking cigars.

GC: Oh, really?

CB: But I quit when I was Director.

[Laughter]

CB: Harold Morris was another senior person in that laboratory, did a lot of work on a group of liver tumors. He was able, through dietary means, to induce liver tumors in animals fairly consistently, and they had different degrees of differentiation so that they became good test subjects for a lot of other people. He supplied these tumors for many scientists throughout the country.

Jay White was more concerned with animal and nutrition studies. He later became head of the Physiology Branch at NCI. He was one of a group that played poker every Friday night. That group included Andervont from the Lab. of Biology.

One of the things I think my education is deficient in is that I didn't learn to play poker.

[Laughter]

GC: Oh, really?

CB: It's good training.

[Laughter]

GC: So it sounds like you got to know people from other labs or other divisions.

CB: Yes. Biology people were on the floor below us in Building 6. We had a lot of joint seminars, of course. Nobody would think anything about going and talking to anybody

you wanted to. There was a good exchange of information and very little negative kind of competition. There was a lot of cooperation.

GC: Oh, really?

CB: In fact, some of the old guard were worried that when the Clinical Center opened, which was in 1955, that this collegiality might not be as good, and they weren't particularly happy to have clinical research brought in. Again, Congress I think, is partly to get credit there.

But Surgeon General Parran, who was Surgeon General up until about 1948, I think—part of his vision for the Public Health Service was to have the Clinical Center in which laboratories and patients were side by side. Under Jack Masur's leadership, the Clinical Center was built with about 500 beds and twice that many laboratories adjacent to the bedrooms. The Clinical Center was a great step forward to blend some of the laboratory work with the clinical side.

GC: Because when you first came there, Building 6—the entire National Cancer Institute was in Building 6. Is that right?

CB: Essentially, plus some space in Building 8.

GC: Essentially. How was it arranged? What was on what floor? Do you remember?

CB: Yes. The radiation work, one of the branches, was in the basement of Building 6 because you wanted to protect from stray radiation. In fact, there was a spillage of radium in one of the rooms, and it took quite a while to get it cleaned up so that it was safe to go in.

GC: Oh, really?

CB: But that helped provide important data in those days for dangers of radiation.

I'm sorry, I'm having trouble remembering the name of the head of that branch [Note: Egon Lorenz]. But he was concerned with radiation biology and its relation to cancer.

A lot of animal rooms were in the basement, as well as in the attic.

GC: In the attic, too?

CB: Yes. On the first floor was Biology. Dean Burk was on the first floor. I've already mentioned that Andervont was the head of Biology. Dean Burk was a famous scientist who knew Otto Warburg, sort of the granddaddy of Cancer Biochemistry. Warburg was invited to spend six months in Burk's lab; so there Warburg was right underneath us. Again, it was thrilling for a young person to go and hear Warburg talk about his work, because he had done some of the first fundamental biochemistry of cancer, tried to show that the difference between cancer and non-cancer was in the way the carbohydrate metabolism took place. It looked very promising in those days, but it didn't hold up as being a consistent general finding.

Walter Heston was another biologist who was a geneticist, and one of those scientists who loved to live right among his animals. When we were later designing a new cancer building (Building 37), in his area he actually had drawn a sketch where his office was literally in the middle of a big animal room because he was so closely attached to his animals on genetics studies. He did important work in the genetics of cancer, particularly on lung cancer aspects—the relation of genetics to tumors.

The second floor was Biochemistry.

The third floor included Wilton Earle, who was one of the two top world leaders in tissue culture, i.e., growing the cells in glass vessels outside the body. He was, shall we say, portly. And one of the funny stories about him was that he wanted a big centrifuge put in on the third floor, and the engineers were saying the floors wouldn't support that much weight. And they said, "This floor will only support so many pounds per square foot." He weighed a lot more than that, so he bounced up and down and said, "Wanna bet?"

[Laughter]

CB: So he finally got an okay from the engineers because he proved through his weight that the floors would obviously support a lot more than they were saying. That was a little anecdote that was kind of funny.

We had a little bit of developmental biology, or embryology, with Cliff Grobstein on the third floor. He later became Dean of the Medical School of the University of California at San Diego. Also he was very active in the social problems such as radiation dangers and

environmental hazards and that sort of thing. And he wrote some interesting books. He has one on DNA and implications in social aspects of DNA. So he was very active, in addition to his laboratory work. Also on the third floor was Emma Shelton. Also, George Hogeboom and Walter Schneider; they were cellular biochemists.

There was one other building (Building 6) that contained NCI people. Murray Shear, who, along with Greenstein, wrote most of the papers in the very early issues of the *Journal of the National Cancer Institute*, made contributions both in carcinogenesis (causation of cancer from biochemicals in a quantitative fashion) as well as the search for and synthesis of therapeutic agents and development of animal test systems.

Joe Leiter, who started out as a technician with Shear and later got his Ph.D., made a lot of contributions with Shear. Later he retired from the lab and became head of Operations at the National Library of Medicine. He did an unusually good job there in management. He's still alive, but unfortunately blind.

GC: Oh, really?

CB: But he still goes to a lot of talks. Unfortunately, we're both going to too many funerals and memorial services. Dr. Marvin Schneiderman just recently died. Leiter was there.

Lloyd Law was another one in this Building 8. He was also an outstanding geneticist and did a lot on the relationship of genetics to leukemia.

Mike Potter worked with him, and developed a line of tumors that led to monoclonal antibody production. When you combined the tumor line that Potter had developed with other cell lines, you could get cells that produced antibodies in large amounts, all of one type. These have been useful particularly in cancer diagnostic research. That goes way back to 1958 or so, I guess.

GC: And you said that people were afraid that things would change when the Clinical Center came in in '53. Was it your impression that the atmosphere of the NCI did change?

CB: No. I think it was an improvement because it didn't do away with the older pattern, but it added on other capabilities. Also you really need to evaluate the laboratory work with clinical work sooner or later. I think it was the right thing to do. We didn't lose any of the collegiality; we just added other types on.

There were a few people that didn't pay any attention to the Clinical Center, but that's all right. As long as they were turning out good research in other directions. There were others there in the Clinical side who were very good at building the bridges, like Tom Frei and Emil Freireich. They had a pretty good grasp of the basic science involved in leukemia, as well as the treating of patients. So I think we built very good science into the Clinical Center activities. And so it was all pluses, as I see it.

GC: Another one of your positions I wanted to ask you about was 1960 to '61 you were Acting Scientific Director. Now, was that between two Scientific Directors? Was it before another one was appointed? Or what was—

CB: Well, Dr. Mider had been Scientific Director, and Dr. Smadel, with whom I worked for for a while in Building 1 at the NIH level, went back to the lab, and Mider was selected to succeed him. That left the Scientific Director job open at NCI.

Dr. Heller was still Director of NCI at that point, and I was Assistant Director at that point, so until they decided who they really wanted for Scientific Director, I acted in that role. But Zubrod really directly managed all the clinical activities, and I managed the non-clinical, although I represented the NCI at Scientific Directors' meetings at the NIH level.

When Endicott came in after a short time, he reorganized and created a new position, which he asked me to fill, called Associate Director for Program. And it was hard to figure out what that meant. And I may have mentioned, it meant what Dr. Endicott wanted it to mean!

[Laughter]

GC: Oh, really?

CB: But one of the main functions was analysis and planning of the total of NCI programs. So I moved to that job and became also member and Executive Secretary for the NCI Executive Committee consisting of the senior NCI staff. Meetings were held every week. Endicott and Zubrod generally set the agendas, and I wrote the minutes and follow-ups. And Zubrod became Scientific Director. And it worked out fine.

So I guess I've covered the main people at NCI in those early days. I'm sure I've forgotten a few. But they really were leaders in those days. Earle was clearly a leader in tissue culture, and Andervont was one of the leaders in the biology of cancer in general in animals. Greenstein highlighted biochemistry, and so on. So we had a good group.

GC: So the NCI was very well-known internationally, would you say, at that time, from the very beginning?

CB: Certainly after they'd been in operation for, say, five years after World War II, it was clear they were leaders. For example, I think six members of the NCI staff have been President of the American Association for Cancer Research. That's kind of a measure of their esteem in the scientific community.

Another thing I've observed: I get a lot of catalogs and brochures about coming to scientific meetings, and in many of those you see NCI staff members on the programs, and I must say I'm concerned, because in the past year and a half, I don't see as many NCI staff members listed like they were earlier.

GC: Oh, really?

CB: I think this is a disturbing sign, but it may not be of any significance; I don't know. It probably depends on who the program chairmen are who set these things up on who's invited to speak. But I have noticed a difference, and I'm not sure what it means.

GC: That's interesting.

One of the interesting things, I think, about your career at the NCI, is that you moved all the way up to become Director.

CB: I had a lot of different jobs, yes.

GC: Yes.

CB: The experience at the NIH level (I was there a year and nine months) was also very good training. I got to know a lot of people in other institutes besides NCI that way since I was Assistant to the Associate Director for Intramural Research, Dr. Smadel. And the reason I went there is that I got asthma from the animal danders—

GC: That's right, you mentioned that.

CB: In Building 6 I literally almost died a couple of times from asthma attacks. I tried wearing a mask and took shots, but that didn't seem to do any good. Finally it was clear that I was going to have to get out of the lab.

I first went to work in the Grants area of NCI with Dr. Ralph Meader. Here is an interesting sidelight: I had a Jane Coffin Childs fellowship at Berkeley, and the Jane Coffin Childs Foundation was based at Yale University, where Dr. Meader was Secretary for that Foundation and Stanhope Bayne-Jones was Chairman of the Foundation. When I was taking graduate work in Berkeley, I got a letter from the Jane Coffin Childs people,

Meader and Bayne-Jones, suggesting that I come and meet them at St. Louis where the Second International Cancer Congress was being held.

So I met them at that time, but none of the three of us realizing that our paths would cross again, because later Meader was Head of Grants at NCI, and I went to work with him, and Bayne-Jones was on the National Advisory Cancer Council.

GC: Oh, really?

CB: It's interesting how paths cross sometimes.

I was in the Grants area for about a year and a half, and I went back to the lab when the Clinical Center opened, thinking I wouldn't have trouble with the animal dander in that building, but I had about as much trouble there. So I was going to go back to the Grants area at NCI, but I got the offer to be assistant to Smadel, who was being brought over from Walter Reed Army Center. He decided that it would be good to have some help from someone who knew NIH, since he didn't know anything about NIH, having been at the Army.

He was considered to be a very tough administrator, and he was. But I got along with him fine. He dressed me down once, but that was all right; I'd made a mistake. But some people were literally scared of him, I mean literally. [Laughter] Their hands would sweat when they'd go meet with him. [Laughter] He was tough, all right, but his standards were high, and he was usually right. And he would change if you presented good information to the

contrary. He wasn't unreasonable, but he was tough. And that was good training, because I was probably not tough enough.

I was Executive Secretary then for the meetings of the NIH Scientific Directors, which Smadel chaired, and also for the NIH Clinical Directors, which Smadel also chaired. So I got good experience on how to run meetings and develop carefully selected agenda items; put time limits on discussion for each; made sure we had clear definition of the decisions that had to be made; then wrote good minutes; and then followed up to see that it got done. That was very good experience.

In those days, I was still pretty young, so I had to be very careful when I went to see some of these more senior people to show that it wasn't my ideas I was transmitting, but it was Smadel's ideas. And you had to make sure that it didn't look like you were taking over something that was his prerogative. That was good training, too: how to deal with people.

GC: So do you think all this moving around to these different jobs, did that help you eventually when you became Director?

CB: Oh, sure, sure. I got invaluable experience . . . not only in working with people, which is essential, but with respect to the subject matter. For example, my first foray into administration was sitting on an NIH board that dealt with the pricing of resources, such as animals. The question was whether you supply animals to the scientists from an animal production within the NIH, or do you do it all by commercial contracting on the outside?

[End Side A, Tape 1]

[Begin Side B, Tape 1]

GC: Okay. We were talking about how to supply animals.

CB: For example, different strains of animals were important for different kinds of research. But you probably can't expect the animal production at NIH to produce every kind of strain of animal because some would be rare and nobody wanted them except one or two scientists. And so you're always balancing the kind of need versus the cost. So who pays for the animals, and how many different strains should you make? So these kinds of balances on the central services are a tricky thing.

This committee was set up to advise those who were in charge of the central services operations on some of these issues. We were always getting complaints, "Well, I can get that cheaper on the outside." Yes, but then if you do that, the capability of the in-house to supply different varieties is more limited. So it was a balancing act, and that was a good introduction to science administration.

Also, that's where I first met Bob Learmouth (pronounced Larmoth, though it looks like Lear-mouth) who later was Executive Officer of the NCI and later of the NIH, and one of the wisest persons I've come across.

He started out working his way up beginning as a government messenger, and ended up as Executive Officer of the NIH. And, as I say, he had wisdom. By that I mean that he could take very complicated situations, distill out the key main points, and make proposals of what should be done. Once he pointed it out, everybody said, "Oh, yeah, yeah!" But before that, often they had a bunch of discussion without anything crystallizing. He was, of course, a very nice person, too. So he was one of the pleasures of my career.

He and Endicott and I then were the three in the front office of NCI who worked very closely on a lot of things. We took what some people would say were too long lunch hours, but we got a lot of business done that way. Morrison often joined us as Assistant Director.

Where are we?

GC: Well, one of the things I wanted to ask you about, when you were Director, how often did you go testify before Congress, and—

CB: Before I was Director, not very much. As Scientific Director for Etiology, I think I testified once or twice; once on tobacco and once on toxic materials, carcinogens.

But I didn't quite finish one thing before this, and that was after I worked with Smadel, I went back to the Cancer Institute as Assistant Director with Dr. Heller. The Assistant Director job is really to assist the Director to do all sorts of things: serve as Acting Institute Director in the absence of the Director; a lot of correspondence was drafted, sometimes for his signature, sometimes for your own; a lot of congressional and other inquiries were

answered; testimony was prepared before the Congressional hearings. I edited all kinds of materials that were going up the line especially in budget, and I consider the budget development a key function. It's one way you can influence direction. I paid a lot of attention to budget, even when I was Assistant Director, but especially when I became Director.

I've already mentioned how I moved from Assistant Director to Associate Director for Program. And that was about six years, but very enjoyable, working with Endicott and Learmouth. And the rest of the staff was top-notch.

When Paul Kotin left as head of Etiology, which of course is the study of causation of cancer, we had trouble recruiting somebody to take that job. So after a fellow from the University of Wisconsin turned us down, Endicott looked at me with his big blue eyes and said, "Carl, what are we going to do?"

I went home and thought about it and said, "Okay, I guess I'll run it myself." So I became Scientific Director for Etiology when we had trouble recruiting somebody else. That was good experience because that was really the first time I had direct line responsibility. The other jobs had really been staff jobs, except in the Lab of Biochemistry.

Endicott then was tapped after two years to head another program at the NIH level. At first I was Acting Director from September of '69 till February of '70, and then I was made Director. A selection committee made recommendations to the NIH Director (and, I assume, the Surgeon General). I usually say I was Director from '69 because I don't see any difference; I acted as though I was Director even when I was Acting.

GC: Right.

CB: Which is the only way to do it really. With the new Cancer Act, the head of NIH and the head of NCI became Presidential appointees, and Mr. Nixon did not appoint me. Dr. Marston, who was head of NIH, was kind enough to invite me to be in his office until I figured out what I was going to do. While there I did a study on how to bring engineers into the biomedical field a little better because at that time NASA was laying off a lot of engineers, and each agency was being asked if they could find jobs for some of these engineers.

That was an interesting exercise because the philosophy and priority perceptions of the engineers compared to the biomedical people were entirely different. The engineers I admired because they often could solve problems without understanding everything that's going on, while most basic biomedical scientists seem to be unable to do much until they understand the mechanism.

I call them different cultural systems. And when you have different cultural systems, you have problems communicating between them. It's not only the denotation of words; more significant are the connotations. But when we talked to the engineers about priorities, they had an entirely different kind of formulation of even the questions, much less deciding.

But I didn't stay very long. I went to head up Hazelton Labs after that.

Yes, I think certainly all these different jobs were very important. Now, you can do it without all this management experience. There have been many examples where an Institute Director was brought in from the outside because of his expertise in usually the area of that Institute's program, and some of them turn out to be good managers, and some of them don't.

I probably paid more attention to the management aspects than most of the others. At Institute Directors meetings, Marston would ask for comment on some subject, and usually only two of us would open our mouths. Ted Cooper from the Heart Institute, who later became head of Upjohn Pharmaceutical Company—well, he was also Assistant Secretary of Health before that; he and I always said something, not always what Marston wanted to hear, I guess—

[Laughter]

GC: But something.

CB: He wanted it, and we gave it to him. [Laughter] And I was surprised how many people didn't say much of anything at those meetings.

GC: Was there a lot of interchange then between the Institutes in terms of—

CB: Collaborative work?

GC: Yes.

CB: Yes, but that was often left up pretty much to the individual scientists, rather than trying to force it from above. But there were examples—and AIDS is a good example currently—where more than one Institute were jointly doing all sorts of things together.

And there were other examples. When I was Institute Director, the Dental Institute had identified a group in South Carolina where there was a lot of inter-marriages, so they had a very interesting genetic pool. The Dental Institute worked all this out in terms of dental problems—it was noticed then by the other Institute Directors that here was a chance to look at other aspects in a genetically-defined population. So there were some collaborative ventures set up along those lines, with the different Institutes. And that was started from above down. Most of NIH research was from the bottom up.

GC: Well, that's interesting.

CB: Well, this is probably the biggest difference in running NIH compared to other agencies. It depends what you're after. I think we get too many arguments as to whether you ought to have planned or unplanned research. Certainly in exploratory research, you don't want central control. You want variety of probing. And so the grants system is the best thing we've come up with, I think, for exploratory research.

There are other activities, as illustrated by the Chemotherapy Program, where you need some kind of central integration. And we keep getting into arguments as though it's either/or, when I think you need both—it depends what you're doing. So some work you need to tie

together different scientific disciplines. You've got to have some kind of integration. Now, you get into fights on whom should that be.

But a lot of people think you ought to do only the grants philosophy, and much of Intramural staff has the same philosophy. The Chemotherapy Program was pioneering in the sense that it broke out of that tradition. And a lot of people were very unhappy about that.

In fact, Dr. Mider really didn't want any of the Intramural people to work with Endicott on the Chemotherapy Program because he was so opposed to that kind of, I would call it, planned research.

GC: Oh, really? Wow.

CB: And others—when Red Stewart, who was head of Pathology, who was also in Building 8, and Thelma Dunn, who worked very closely with Red Stewart—and both of them were Presidents of the Association for Cancer Research at different times—both of them really have written opposing the idea of planned research and commending Dr. Mider for his stand against it. [Laughter]

Now, it's nice if you have the individual scientist do whatever he pleases. In fact, Red Stewart—I never did find out how serious he was—in his Presidential address, proposed that a big pile of money ought to be available for the scientist to go and draw from whenever he needed money.

[Laughter]

CB: No priorities at all!

[Laughter]

CB: That's an extreme view. As I say, I couldn't tell whether he was serious or not! [Laughter] He sounded serious. [Laughter]

GC: He probably was.

[Laughter]

CB: Incidentally, I went to his 95th birthday celebration. And he was still working.

GC: Is he?

CB: At 95, yes. He was one of the more colorful figures there, as was Dr. Mike Shimkin, who headed the field investigations efforts at one point.

Incidentally, when I came into the Public Health Service, we had both written and oral examinations. And I was at Berkeley, and there was a PHS hospital in San Francisco, and Shimkin was heading a clinical investigating unit at Laguna Honda Home, it was called. Well, Shimkin and the executive officer of that PHS hospital were on my oral examining board.

GC: Oh, really?

CB: And I'll never forget the question Shimkin asked me: "What was Count Bernadotte's plan for Israel?" [Laughter] And I said, well, I knew he had a plan, but I couldn't relate the contents of it.

[Laughter]

CB: And then the other guy asked me to explain Einstein's theory of relativity. And I started to explain it, and he said, "Well, nevermind." He didn't understand obviously what I was saying! [Laughter]

GC: He just wanted to test you?

CB: I could make a fair stab in those days explaining what it was.

[Laughter]

GC: Oh, my gosh.

CB: Well, I don't know how many of these anecdotes you want.

GC: They're great!

CB: Well, they're fun. [Laughter] I don't know whether they're any good for your purposes, though.

GC: I did have some other questions.

CB: I hope so.

[Laughter]

GC: When you were Director, the position was not yet a Presidential appointment, correct?

CB: Right, before the signing of the Act.

GC: Right, exactly.

CB: And that was signed in December of '71.

GC: Right. Now, did you have any contact with the White House or the President the way the Directors since then have had?

CB: Yes, I had some very interesting contacts.

GC: Like what?

CB: Well, from my point of view, the planning exercises I felt were most significant. But I also had a lot of contact with the Secretary of HEW in those days. And I did have one face-to-face meeting with President Nixon when he went up to Fort Detrick to convert the Germ Warfare facility to the Cancer facility. Right before he gave his talk announcing this, we briefed him on the current programs of the NCI. So I took Zubrod and Rauscher with me, and they both presented a good front and talked well. I covered the general aspects of cancer and everything except Viruses Cancer, which I let Rauscher cover, and the treatment side, which I let Zubrod cover.

And it went very well. There wasn't anything earth-shaking that came out of it, but it was an interesting experience.

And on the political activities that went on prior to the signing of the Act, we were quite active, and I was involved in that in several stages, including testifying in part. I don't know how much detail you want of that. I'm writing an autobiography, and I'm going into a lot of details of it. And then there's a book by Strickland that covers the political activities quite well.

GC: *Politics*-something-*and Dread Disease*? Is that it?

CB: Yes. There's another one by Rettig (not as good as Strickland's). One of those books describes all the political activities very well and in considerable detail. There was a hassle between Nixon and Kennedy on who was going to get credit for giving more money to cancer.

GC:[Laughter]

CB: And then you got into a lot of side issues, like Mary Lasker and Sidney Farber and her group, and the panel that was set up with congressional action. They wanted to pull the cancer program out of NIH. Now, that set the academic community against that idea.

So the Senate had gone along with what Mary Lasker wanted to do, but Congressman Rogers in the House, who was getting a lot of input from the academic community and the scientific societies, decided he was going to go his own way and write a whole new bill and have hearings really quite different from the hearings in the Senate.

There's a lot of information on that available.

GC: Yes. We probably don't need to go into all that.

CB: And I was <u>indirectly</u> involved in that. One of the issues that Senator Kennedy raised was, did we have any planning, "You don't have an overall plan, do you?" And I had to say no, because even though I had an overall plan, but it hadn't been approved. So I probably made a mistake by answering no when I should have said, "Yes, I've submitted one in channels," in February of '71, actually.

I had outlined a total expanded program which was proposed to go to a billion dollars a year. This seemed outlandish in those days, but of course they're over two billion a year now.

GC: Right.

CB: And I answered that we had pioneered planning in the viruses area and the chemotherapy area. "But you don't have one overall plan, do you?"

So that was a little misleading. But I was being a good executive branch member by saying, since it wasn't approved, that we didn't have it. I think that was a mistake, probably.

GC: But it's hard to know.

CB: It wouldn't have made any difference anyway, in the long run.

GC: Right.

CB: Also, when I told Mary Lasker directly that I was opposed to pulling NCI out of NIH, her relations with me cooled quite a bit.

GC: Because you opposed her?

CB: Because—yes. Well, I suppose she felt that why do you want somebody to head a program if they don't believe it should be pulled out if you are trying to pull it out? But, of course, the issue ended up with a compromise with the President's Panel. That was all done to—it was a compromise between the Kennedy forces and the Rogers forces, shall we say . . . Mary Lasker being with the Kennedy side.

So the administration kept changing proposed bills through all this. And Kennedy asked my opinion on one of the bills, and I hadn't even seen it! [Laughter] It had only been written about two days before, and it hadn't gotten to my level.

And Steinfeld was Surgeon General, and he had been NCI Deputy Director, so he knew a lot about cancer. So he was handling all the formal technical testimony. I was sitting back in the audience.

So Kennedy—no, I guess it wasn't Kennedy—it was Anchor Nelson who asked me what my views were on the (latest) bill, and, since I hadn't seen it, I figured I had better punt. I tried a joke which didn't go over too well, I guess.

GC: Oh, no.

CB:I was like a statistician who was asked how his wife was, and he says, "Compared with whom?" [Laughter] Well, that's what I meant by all these bills being involved when I hadn't seen the latest one that they were supposed to be discussing. And neither had some of the members of Congress, including some on the Hearing Committee. It was a very confused area in that sense. And it was all jockeying for who's going to get the credit here?—which is not surprising in politics.

GC: Sure. It must have been fairly interesting though, the whole process.

CB: Yes. But I not only had planned, but this circular chart I gave you indicates the structure of the plan. We had over 200 scientists we got together to help look at all this. And so I

think if I'd stayed in the job longer, we could have built on that rapport that was started at the Airlie House meetings. Because while I believed in planning, I wasn't trying to do it all by myself. I was inviting all these comments from experts in the different areas, but you had to organize that somehow, and that's what the chart is all about really.

If you look in the middle of that chart you will see the overall goals. And then there are the main efforts for reaching those goals. And the outside periphery are actual research projects. And we weren't trying to tell anybody how to do their research projects. But I found that even very good and senior scientists had trouble understanding what we were talking about in the intermediate areas, which I call program areas. They understood the overall goals easily, and they understood the project level. But what's a program goal?

Well, again that's because most of those people never had to put budgets together for something as big as those of the Cancer Institute. There we divide the budget into program areas like chemotherapy, etiology, intramural versus grants, and so on. There are two kinds of programmatic aspects, the more important one being the scientific basis. But you also have to look at the managerial/administrative categories.

GC: Right.

CB: But anyway, the conceptual aspects are very different on how you look at it at the project level compared with the program level. Most of those people hadn't had any experience with program levels, so they had trouble really understanding what we were talking about.

GC: And grasping that.

CB: I believe that would have been worked out all right had we had the chance to continue the orientation and review sessions with leading cancer investigators.

GC: What do you think your greatest contribution was over your whole time at the NCI? What were you proudest of?

CB: Well, the planning first, and second the creation of the Organ Site Programs. The reason for that was because when I became Director, I looked at the various levels of funding in different aspects of the cancer programs, and found that we only had nine grants totalling $212,000 on large bowel cancer. Now, you put male/female statistics together, large bowel cancer is the biggest category of death. At least it was then.

"How come we've got such little effort in this?" I said, particularly to the Grants staff. "Well, nobody knows what to do." "Oh?" So I went in the NIH library, and in three nights discovered that we had an animal model where you could produce large bowel cancers experimentally. You give me an animal model, I can build a program around that.

[Laughter]

CB: So what I did was set up groups that were expert in, in this case, large bowel cancer, and were interested in doing something about it. The study sections didn't have people of that nature sitting on them. That's why a lot of the proposals were turned down. So I established these groups, first with large bowel, then with urinary bladder, then prostate,

then, preliminarily, pancreas. In each case, I established a group of experts in the particular area and selected the Chairman for each.

I didn't really think that I would get this established so easily. I thought surely the Division of Research Grants would object to our (NCI's) establishing another review mechanism instead of using the conventional Study Sections. But they seemed to be glad to get rid of this applied area. As they saw it. So I didn't have any resistance at all, which surprised me.

GC: Amazing.

CB: Interesting little sidelight on how you fund it, too. I studied strategy and whatnot in wartime a little bit because I considered this was a war we were fighting against cancer so we should fight it like a war (which we were not doing and still are not doing, in my view). And I looked at what was done in World War II, for example in dealing with tropical diseases in the Pacific.

Troops were going into areas where there was a lot of tropical diseases, which most didn't know much about. But there were a few experts in the country who knew a lot about such diseases—Smadel, for example, was one who knew a lot about some of those diseases. In the Army, that's what he was partly responsible for.

But there were five or six people that were really knowledgeable of that area of medicine, and similarly there were some real experts in large bowel cancer.

I said, "Well, why don't we do it like they did it in World War II on the tropical disease problems?" They would get three or four people who were the top experts together, give them a bag of money, and say, "Here, go solve this problem." It seemed like a nice effective way to move ahead.

[Laughter]

GC: Sure.

CB: Oh, no. Members of the National Advisory of Cancer Council would not hear of this approach. I wanted to even do it with grants because I didn't have any more money in contracts that I wanted to use. And of course with grants, you have to have formal approval from the Council to make a grant. (You didn't have to with contracts; we got in a fight with Mary Lasker over that one.)

But I remember very well, one of the Council members, when I proposed all this, looked me in the eye and said, "Well, you can try that if you want, but it won't go through." And I knew he was right, that I wasn't going to get that one through.

So we had to do it within the regular grants review system—it got done, anyway. So now we have a lot of good work in large bowel cancer. This is an example of adding on, not replacing, the grants philosophy. I'm a full backer of the grants mechanism (for exploratory basic research), even though a lot of people probably didn't think so because I kept talking about planning. This, I think, was an add-on that has done a lot of good for focussing on major cancer problems.

Again, it probably makes a difference which end of the spectrum you're starting on. If you're looking at an allotment here for discovering basic research findings that we don't know anything about, that's one end of the spectrum.

The other is like here, "Well, we've got a large bowel cancer problem. What do we do about it?"

GC: Right. It depends on how you approach the scientific problem.

CB: Yes. And so the overall planning ties them together and deals with both ends and the middle.

GC: Which is why—didn't you call it convergence planning or convergence technique?

CB: Yes. So I think those two things, the Organ Site Program and the planning efforts were my best efforts. The planning hasn't really been accepted very well. The chemotherapy people not only accepted it, but are still using the same ideas in the flow charts that I gave you last time. But the virologists—we might has well not have done the planning, except it was good for us to learn how to do the planning.

And then the chemical carcinogenesis was in between. They used it partially, e.g., as a help in budget justification. After I left, Carrese and a couple guys did a basic immunology program flow chart, but that never took hold either, I don't think.

So I think it's unfortunate that we keep treating this as either/or, when we really need some of each. And maybe we have that still.

GC: Probably. I wanted to ask you about your oral history project on the Virus Cancer Program. What prompted you to start doing that?

CB: Well, I just think that NIH by and large needs more history written, for two reasons: one, I think we ought to honor some of the great contributions that were made by NIH staff and the staff. And so one purpose of history, I think, is to do honor to people who made contributions.

GC: Sure.

CB: And secondly, it's pitiful, the lack of knowledge of previous activities. Such ignorance affects how you run an organization. And an organizational memory, I think, has more importance than a lot of people give it credit for.

GC: I agree.

CB: And history is part of that. And so I just thought we needed more history writing about NIH. The viruses-cancer was one area that I was very involved in and knew well and thought was very significant in laying additional foundations for molecular biology and biotechnology. And people ought to realize it. This was very important and ground-breaking in developing techniques that we're using today in AIDS and in biotechnology, and there ought to be recognition of it. And maybe you might even learn to think more broadly if you read a little more history. [Laughter]

GC:I think so.

CB: Oh, I imagine you agree with that, yes.

GC: It's interesting. Everyone I've talked to has mentioned how important the Virus Cancer Program has been, but they've also said that there was a lot of criticism of it. Now, was that true at the time, or was that later on, like when the program was first started—

CB: Negative criticism was starting about the time I was no longer Director. The biggest criticism had little to do with the scientific output. It was concern that some individuals had too much power and control over sizable chunks of money, primarily Huebner.

GC: Really?

CB: In terms of fighting a war, I think we ought to be looking in a very different way at the contributions Huebner made. I called him my "General Patton," because he was like a general because he had several contracts which he tied together into a major effort. And therefore, the research capability of that group under Huebner's jurisdiction and leadership was like a general with several subunits working together.

Now, what's wrong with doing research that way? In industry, they're used to this. But the academic community is not used to this. So they felt that Huebner, and Moloney, too, I guess, had too much power, and this was bad, unfair.

I've learned that fairness is an enemy of efficiency.

[Laughter]

GC: That's an interesting way to put it.

CB: But you've got to have safeguards, but too much of detailed safeguards is obstructive.

So, anyway, this led to—there were enough complaints that the National Advisory Cancer Board (after I left) as usual, set up a committee under Norton Zinder to review the cancer-viruses program. I never have seen the actual report. All I've been able to read is reports about it. As near as I can tell, they were fairly complimentary to the science involved, but were objecting to the review mechanism. And, as Moloney puts it, it led to the demise of the program.

There are other reasons; namely the opposition to planning in general. I think the President's Panel, i.e., Benno Schmidt, under our urging accepted the planning originally. But as time went on people in the academic community and his colleagues at Sloan-Kettering Memorial kept talking that you needed more money in grants rather than in contracts. I think that also led to the demise of the program, shall we say.

GC: Now, did it end? Did all viral oncology work end?

CB: Oh, no, no.

GC: Or just that program ended?

CB: Well, in the some sense it ended. They still have some contracts in viral cancer work, which of course, makes a lot of sense. In some areas of producing resources, the academic community doesn't want to fool with large-scale production of resources.

Certainly one of the contributions of the Viruses Cancer Program was in the resources area. At the time we started it, you couldn't buy many of the resources needed; many were not available or were in insufficient amounts. There were individual virologists who made certain reagents and whatnot in certain animals, tissue culture and cell lines, but as I told them, "You fellows are very good about exchanging samples to check on the validity of the materials, but by the time you have exchanged your samples, you don't have any left to work with. So we need to produce much larger quantity. And industry is the way to do this."

"Well, they won't make it pure enough." "Oh? Well, look. You can test it the same way you've been testing your stuff, and obviously if it's no good, we're not going to force anybody to use it."

GC: Right.

CB: So we had to get over that hump of the attitude.

GC: Was it kind of a distrust?

CB: Well, "industry can't make it good enough. We're the academic experts," and all. And I knew I was over the hump when Moloney came in one day and said, "We just got a batch of one of the viral preparations from Pfizer, a contractor, and it's as good as anything we've ever made. And we got buckets of it."

[Laughter]

CB: But it took a while to get the scientists to accept this. I don't know exactly why, but the attitude was there. Now a lot of resources are commercially available, but they grew right out of the pioneering work of the resources developments in the Viruses Cancer Program.

Two people there were key in getting that through. First, Harvey Scudder, first as Executive Secretary of the Virology and Rickettsiology Study Section, and later he moved to the Cancer Institute with Ralph Meader in Grants—he perceived this need to produce larger quantities of resources which were standardized and evaluated for quality. This resources development actually started out with grants. That was a very unusual move. However, due to a lot of factors, Endicott switched all that from grants to contract-supported operations.

Second, Bob Stevenson ran that program after Scudder left. Those two were very good in initiating the actual provision of resources that were unavailable commercially and were not going to be developed until there was a market, of course. And so we did a lot of developmental research, really in there, in animals, including primates, tissue cultures, cell lines, viral reagents.

And then communications—we had a lot of meetings where information was exchanged, and it got to be freely exchanged. Unlike the problems of arguments about who published first, these annual meetings became a good place to go and get updated, and people communicated what their current work was. And I think another contribution of those programs was in the communication area.

And Bob Gallo is still following this same pattern that he learned in the Viruses Cancer Program of having annual meetings where the experts in the area get together and tell about their current status and discuss problems: "Where are we going next, fellows?" That kind of thing.

So we really did have a lot of participation. It wasn't just the staff doing this, although they did a lot. And so the concern that there's too much power with too few people, I think was an unfortunate development, but it's not surprising.

GC: I don't want to—since you're already doing a lot of virus cancer oral history interviews, I don't want to overlap you too much.

CB: Well, I wouldn't worry about it.

GC: Okay, all right.

[End Side B, Tape 1]

[Begin Side A, Tape 2]

GC: Okay. So we were talking about the Virus Cancer Program and about how the communications was another aspect of it that was very important. Did we cover everything there?

CB: Well, I'll make one other point. On the resources, for example, animals . . . even today we import a lot of the monkeys, and so many of them have diseases. We, at one point, thought we were going to need a lot more primates for testing human specimens for cancer-causing capabilities. So we looked at the problem of producing monkeys in captivity, and put a lot of developmental research money into that. Because we didn't even know what the normal blood-count picture looked like in these animals.

GC: Oh, really?

CB: And didn't know what the best nutrition was, and the conditions of keeping, and whatnot. So we developed the area to a point where we could produce all the animals we needed without having to import any. This got rid of a lot of the disease problems we had. So if we ever need to produce monkeys, we know how to do it, if people don't forget the history.

GC: There's a good point right there. Now, the people you're interviewing [for Dr. Baker's oral history project], have they been bringing up things about the Virus Cancer Program that you didn't realize, or have you found them—

CB: Well, one of my questions I asked each one was, "What would you have done differently."

GC: Oh. That's a good question.

CB: Yes. And most of them didn't answer, but a few of them did. One, I remember, was the interesting wording, that we should have "stroked some individuals more carefully."

[Laughter]

GC: Oh, really?

CB:I thought that was a pretty good way to put it.

[Laughter]

GC: Did you answer that question in your interview? Because I noticed you were interviewed.

CB: Yes, I think we probably didn't pay quite enough attention to public relations, as it's called. Scientifically, I thought we were on target all right. And, like Shannon, I think that the scientific issues are the more important ones. These other things on administration and political activities . . . they're usually distractions.

[Laughter]

GC: Right.

CB: Like the requirements now for getting a contract, the proposals now are getting telephone-book thick with all the rules that have been added on. That's why I use the word "obstruction." Even the paperwork to cover the proposals sought with guidelines and rules and regulations is sometimes almost as thick as the submitted contract proposal.

[Laughter]

CB: My wife was in contract negotiations, and I used to fuss about how that interfered with getting on with the science. [Laughter]

GC: Was she in the NCI or in the NIH?

CB: The NCI.

GC: So did you work anywhere near her? Were you in the same building or anything like that?

CB: No.

GC: Did you have any contact with her?

CB: She was down in the business end of things. I didn't get into that area.

GC: You didn't. Now, when you were Assistant Director or Director, did you have daily contact with the researchers at all? Or were you—

CB: Sure. In fact, I had a habit of wandering around and walking into labs and talking to people.

GC: Oh, did you?

CB: Asking questions. Somebody told me I was known as the guy who was always asking questions.

GC: Oh, really? That's interesting. That's probably a compliment.

CB: You had less time to do it at the higher levels. In fact, Smadel one time said I was just like a little puppy dog going around talking to all these people. [Laughter] And I said, "I can learn things that way that you can't learn."

[Laughter]

GC: That's true.

CB: So, yes, I considered that an important communication device. And then I got along with my program leaders, I think quite well, because before testimony on the budget, I would always sit down with each one of them and find out what his priorities were. So when I developed the budget, I knew what they wanted to do. And, as long as you treated them all fairly—here fairness is important—and they knew you were doing that, they realized I wasn't going to get everything they wanted, but I would try and take into account their priorities. So we got along fine, I think. From my view, we got along fine. I hope they thought so, too.

GC:I haven't heard any differently.

[Laughter]

GC: Did you ever make rounds or do anything at the Clinical Center while you were—

CB: No, see, it had been so long since I'd seen patients, I didn't see much point in my making rounds. I went to a lot of lectures that included the clinical side, and I certainly paid a lot of attention to chemotherapy content. So I think I kept up fairly well in the various areas. But I didn't see much point in my making rounds.

Now, DeVita, for example, came right out of that area, so he just continued right on with his rounds all along.

GC: Right.

CB: And, as I say, I paid probably more attention to the management aspects than most of the Directors.

GC: So what was a typical day like for you as a Director? When would you get to the office? What kind of duties would you do?

CB: Well, I would say the variety of inputs was very high in all of the Institute Directors' jobs. One minute you're dealing with Congress, and the next minute you're looking at the

science in great detail and trying to keep up with the latest important findings. Budget took up a lot of time. I spent a lot of time with the Budget Officer, who was another fellow with a great deal of wisdom; Browning was his name.

You would get a lot of phone calls, occasionally wanting advice on where one could get the best treatment. For example, the way I got into the Ludwig Institute was a call from Senator Jackson from the State of Washington. He said he had a wealthy friend who was afraid he had stomach cancer. Could we see him? I said, well, we could see him, we'd be glad to, but we didn't have any special program in stomach cancer. And my best advice was for him to go to the Mayo Clinic. I knew the head of Gastroenterology at the Mayo Clinic, who was on our Advisory Cancer Council; I'd be glad to call him.

So that led to creating the Ludwig Institute. So Hugh Butt and I (Butt from the Mayo Clinic), and I started out the Ludwig Institute that way.

Crackpots, when I was Assistant Director, took up a lot of time.

GC: You mean from the public, or . . . ?

CB: Yes. Andrew Ivy and Krebiozen was a bad one. Senator Paul Douglas, a very powerful Senator from Illinois, was a friend of Ivy's and was backing Ivy, and kept browbeating us, wanting us to test Krebiozen. Our policy was that we had to either know specifically chemically what it was or have its preparation in sufficient details that somebody else could repeat it. And Ivy never met that, of course. And it ended up that Krebiozen was nothing; it was a name; so how are you going to test a name? Some samples had nothing

in it at all except the solvent, and others had creatinine in it. But I'll give credit to the FDA inspectors. They finally collected enough data to show that it was no good. It's much harder to show it's no good than to show that it is good.

GC: Really? To prove it.

CB: You've got to get more data, yes. So they finally had enough cases that it was obvious it wasn't doing anything. But the reason it wasn't doing anything is there wasn't anything there, really.

[Laughter]

GC: But that took up a lot of your time?

CB: Oh, yes. I dictated all night a kind of a history of this area, as I remember, for Senator Douglas—he had to have it the next day.

GC: So you dictated all night?

CB: Yes.

GC: Oh, my gosh. He just called you one day and said, "Tomorrow I want—"

CB: He actually called Endicott. That was when I was Associate Director. So I got the job of doing it, of course, but that's part of the job. Yes.

So it was—high variety, I guess, would be the most striking thing about the job. When I first became Director, every afternoon at four o'clock I'd receive a stack of papers to sign off on. These were every grant and contract that had been awarded that day. And even then we had to spend a million dollars a day or so just to spend the budget.

GC: Oh, my gosh!

CB: Well, I thought that was a silly way for me to spend my time. So I delegated sign-off down to Brandner who was the financial management guy I had for contracts, except those $1 million and above . . . I would sign off on those. And the basis of signing off on them for me in the first place was because Brandner's signature was on them! [Laughter] So I didn't see anything wrong with delegating that authority down, and I got away with that without anybody objecting. So that seemed a better way to spend my time. It would take you twenty minutes to sign all these . . . !

GC: Sure.

CB: Or longer.

GC: Because you would have to at least look at it, right? And see what it was you were signing.

CB: You didn't <u>have</u> to, but I suppose I did.

[Laughter]

GC: Probably a good idea.

CB: But after I while I got to say, "You know, I'm depending on Brandner's signature on most of this because I can't just look at this and decide without going into it further, so I've got to trust it to someone."

In fact, one of the nice things about NIH in those days, the staff trusted each other, so you could rely on it. I mean, we had good people who were just as interested in quality as you were. You can manage a lot better if you've got trust. But you're in a pickle if you don't.

GC: Yes, I guess so.

CB: Look at the D.C. government.

GC: That's a whole other history. [Laughter]

Someone else I wanted to ask you about it Phoebe Dunn. Was she your secretary, or did she come later?

CB: No. She was Rauscher's secretary.

GC: Okay. I wasn't sure if she had started with you or with Rauscher.

CB: No, Rauscher.

GC: Now, did you have a secretary?

CB:I had two or three . . . or several, over the years, of course.

GC:I'm just looking—

CB: Susie, Susan Hooks, was one of them. She was "Little Susie." I had another one who was "Big Susie" (Susan Conners).

[Laughter]

CB:I'm ashamed to say their names don't come right to the tip of my tongue.

GC:I'm just thinking about people I might want to interview in the future, and Phoebe Dunn's name came up, for example.

CB: Betsy Hooks was a sister-in-law of Susie Hooks. She was Endicott's secretary. Bobbie Rother was my secretary when I was in Etiology, and she, of course, was a little unhappy when I moved to the Director's office that I didn't take her with me but kept Endicott's secretary on.

Janet Fisher, earlier—much earlier, when I was Assistant Director. They were all very good.

GC: Do you think any of them would be someone I would want to talk to about the history of the NCI in general? Do you think they had a good view of what was going on?

CB: Betsy Hooks was Endicott's secretary and then mine for a while, and then she was replaced by Little Susie—they were both quite sharp, and the job gave them perspective of the total Institute. If you're interested in that perspective, yes, either one of those.

GC: Okay.

CB: There were some secretaries and administrative people down the line, who (I later learned) complained that these two girls were trying to run everything.

GC: Oh, really?

CB: But I wouldn't take that too seriously. You know, you had to protect the Directors' time from irrelevant intrusions, of which there were many. So Betsy Hooks was a tough cookie to get through sometimes.

GC: Oh, really?

CB: Yes.

GC: You probably appreciated that, though.

CB: Well, I—yes. It's very hard to be in that job without raising those objections. So they were all right. I thought they were fine.

GC: Was there anyone else that you think I should talk to in particular that we haven't mentioned?

CB: You're trying to interview all of the living Directors?

GC: Yes. I've gotten all the living Directors.

CB: You've already done?

GC: Yes.

CB: But unfortunately you didn't get Rauscher, I guess.

GC: No, he's gone.

CB: Or Heller?

GC: No. I've just been working on this this year, and they've both been dead a little while.

CB: You're aware of the anniversary issues of JNCI of 25th year and 40th year or something?

GC: Yes.

CB: My paper on that 45th thing on planning is I think fairly well done.

GC: Yes. You gave me a copy of that, too.

CB:I thought I had.

GC: Right. I think it's very well done.

CB: Cal Baldwin was Executive Officer of NCI.

GC: Okay. He's a name that Dr. Zubrod mentioned.

CB: Yes. You might want to get his perspective. He ended up as the Executive Officer of the NIH, as did Learmouth. The Cancer Institute was the spawning ground for all sorts of good things.

GC: It sounds like it.

CB: Well, it was. I just interviewed Emmett Barcley last week. I hadn't planned on it, but I ran into him at somebody's retirement, I guess. So I realized he had had a lot to do with the safety aspects of the Viruses Cancer Program. He's now at the Howard Hughes Foundation.

GC: Oh, okay.

CB:I don't know whether that would do you any good or not, probably not too much. But he was good on some of the safety aspects. But if you want, that's a possibility. He's over at the Howard Hughes facility there at Connecticut Avenue.

GC: Right, I know where that is.

CB: The reason he comes to mind is that Endicott had an appreciation of the engineers. I think he had a degree in engineering instead of a Bachelor of Arts degree. But anyway, he put some cancer money to help some of these engineers to get additional training. Emmett Barcley was one of those people, and got his degree in Health Sciences with a minor in Microbiology, a Ph.D. on cancer money. Endicott and Learmouth were very good about training aspects.

When I was with Smadel, I went to a lot of training things on computers and planning. In fact, one of the best courses I ever had dealt with systems planning and systems analysis. I was very impressed that they cited a military contract of $2 billion a year, where every Monday morning the guy in charge had a status report printed out from computers on his desk. He would know the current status of a $2 billion project. That was pretty good management.

GC: Yes, that's pretty amazing. It must have been a big printout.

CB: So that's an area that I never got finished. I just barely got started: the information flows against the cancer planning. What I wanted to do in the long run was have information

that was related to the plans, scientific information primarily. But as far as I got on it was that I gave a paper at the International Cancer Congress in Florence on the ideas. But I never got through the development of the system, because after I left Hazelton I was a consultant for a while, and I was a consultant to the TRW that had the contract for developing management information systems for NCI. But the Project Officer at NCI had no grasp of what we were trying to do. That was the first time I ran into somebody at NIH who really didn't know what he was doing. The project died.

GC: Oh, no.

CB: And I wasn't used to that kind of inadequacy.

GC: So as a consultant, you actually were involved with NCI again?

CB: Through TRW.

GC: Through TRW. And I just want to clarify what you said a minute ago. You said that information flow is against National Cancer Plan? Is that what you said?

CB:I don't mean against in an adversary way. I mean you compare your information flows with the plans. In other words, the flow of information ought to somehow be related well to the plans and your proposed managerial scientific pathways.

You look at the total program as a process. And you've got movement of information through there. Well, how do you relate that flow of information to the plans and your objectives?

GC: Okay, I see what you mean.

CB: But one of the advances that we made on our planning of the Chemotherapy Program area versus our earlier one in Viruses, was our introduction of decision points and monitoring points. And on the decision points, we actually stated the kinds of data you had to have to make the decisions, which I thought was a very good addition.

GC: Right, yes.

CB: And the monitoring point, you may have to change your whole flow. So periodically you would review the monitoring points to see if you wanted to change your pattern, your plan. So the planning itself called for frequent update, which it should do. But a lot of them don't.

Another one that was very different was the ends ought to be stated in such ways you can tell when you've gotten there.

[Laughter]

GC: That seems pretty basic.

CB: Well, but most plans say, well, you know, we're going to increase our efforts. What does that tell you?

GC: There's no quantification.

CB: Yes. So I thought in our Chemotherapy Program planning, we introduced these concepts that were important. Now, the hardest point about the planning is, in research, you don't know even if things will succeed, much less when. While the way most of this systems planning has been done is—if you put more money in, you've got a better chance of increasing the result. But we can't guarantee that in research. So time has to be looked at in a much less quantitative way in research program planning, but we always wanted to make sure that people doing the program were well aware that time is a very critical part of the process. Just because we can't quantify, doesn't mean that you forget about the time.

GC: Doesn't mean you can just go off.

CB: So we paid attention to time, but we couldn't quantify it in the same way you would with a construction project or even making a bomber, which is bigger than making a building, I think.

GC: I think so, too.

CB: Have you got any more?

GC: I think that's about it, because we covered a lot in the first interview.

CB: I probably repeated some.

GC:A little bit. Not too much, actually. You added a lot of new information.

CB: Well, there's, of course, a lot more there.

I'm on my last chapter of editing the text of my autobiography. I've got a big labor job of formatting. I've forgotten some of my computer processes. I'm going to have to go back and review.

So I'm afraid it's too long. My longest chapter is when I was Medical Director at Ludwig, because I did a lot of travel with these world-wide things, so I've got all this travelogue in there and description of a lot of churches. And I may have to pull a lot of that out, because that chapter is over 300 double-spaced pages.

GC: That chapter is?

CB: Yes.

GC: How long is your autobiography?

CB:I haven't added it up yet, but the next longest chapter is when I was Director of NCI, and the next one was after I was no longer Medical Director of the Ludwig Institute. So it's way too detailed, I suspect.

GC: Wow. Now, are you going to publish this, or is this just for your use?

CB: Well, I have a vague idea of doing publishing, but I'm not trying to make any money out of it.

GC: It's perhaps just for you, then?

CB: The question is whether anybody would be interested in reading it. And my purpose partly was I've had such an interesting life, why people are bored seems so unfortunate. And so I'm describing a lot of things just to show how interesting the world is, and you shouldn't be bored.

GC: Right. If you're bored, you're doing something wrong. Right?

CB: Well, it's so sad, because some people don't even know there's an option against being bored.

GC: That's true.

CB: And, of course, reading has been the key to this, but the Internet now offers some very interesting possibilities that reading covered. But people won't read now because it takes more time, and they weren't taught to read, really.

And I think my main reason is that, plus I wanted to get the history done because I thought it was important.

GC: Well, I think people are going to be interested in your autobiography just because of the history that you're going to include there.

CB: Well, I don't know. Some people ought to be interested in knowing what in the world does a research administrator do?

GC: Yes, absolutely.

CB: But not very many people find that a burning issue.

GC: Well, I think anybody who is researching the NCI will be interested in reading it, just because, as you said, you've had so many positions.

CB: Oh, if I have an index, the first thing they'll look up is their name in there.

[Laughter]

GC: That's true. Well, like you said, you have to give honor to people, right?. So that can be part of their honor.

CB: Well, one reason it might not be very interesting is I don't have any nasty stuff in there, and I don't have any sex in there.

GC: Oh. Well, that's okay.

CB: I don't believe in telling everything.

GC: That's probably good.

CB: It wasn't difficult to write that without negativity because most of it was not negative. We had some wonderful people that I've worked with.

GC: It sounds like it.

CB: Very few clinkers. I've mentioned the one.

GC: Right. Well, should we end this? We should probably end the interview.

CB: I'll mention a couple more. [Laughter]

GC: Okay. This is ending the interview with Dr. Baker on July 9, 1997.

[End of Interview]

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