

# **Dr. Nathaniel Berlin Interview**

Office of NIH History  
*Oral History Program*

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Interviewee:       Dr. Nathaniel Berlin

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BSP: This is Buhm Soon Park. Today is April 9<sup>th</sup>, 2004. This is an interview with Dr. Nathaniel Berlin at the Office of NIH History on the subject of history of NIH intramural program, especially focusing on NCI's program.

BSP: Thank you very much Dr. Berlin to have an interview with me and do I have permission to tape it?

NB: Of course.

BSP: Okay, thank you very much. Shall we start with your educational background?

NB: Sure.

BSP: Briefly, what kind of funds did you get when you attended the medical school at Berkeley pursuing your Ph.D and why did you take a follow the course of the MD along with Ph.D.?

NB: When I went to medical school most of my time in school I was in the Army. It was the Army Specialized Training Program. It was created during the war.

BSP: Oh, I see it's kind of like ROTC now?

NB: It was – almost everybody in medical school between '43 and '45 was either in the Army or the Navy as enlisted people and that was – they gave us a – they paid our tuition, gave us all what we needed to do our studies with allowances and that was convenient. The first third of my medical school my family provided support for me, and in college I was supported by my family. I went to Berkeley and I finished my internship.

BSP: What year?

NB: It was in the Spring of 1946. We had 9-month internships. I was called up for a physical exam for active duty in the Army and I couldn't pass the physical and then I took a residency in pathology.

BSP: In the same medical – in the same hospital?

NB: Yes, King's County Hospital. And in the Fall of that year, 1946, I saw an announcement in the *Journal of the American Medical Association* that there was a new division created in – or a new program in the department of physics at Berkeley called medical physics. Before I was admitted to medical school I was admitted to graduate school at Case-Western in the physics department. It was in the physics department that I had my best academic performance. I took six courses and had six A's and then physical chemistry I got two A's. So, wherever physics was I did well.

So, I went to Berkeley and when I got to Berkeley in June it was, I quickly learned from John Gofman who was also on the faculty. We were both out of medical school the same year, but John already had a Ph.D. in chemistry with Seaborg and he pointed out to me that the NIH was offering fellowships. So in the Fall of '47 I got to Berkeley in June of '47 – in the Fall of '47 I applied for a postdoctoral fellowship and in the Spring of that year, '48, I was awarded a NCI postdoctoral fellowship. It finished me through graduate school and, when that fellowship was over, Don Lawrence made me a minor member of the staff. Why did I want a Ph.D.? In the crass way it's a tuition receipt and it's cachet. It didn't – from the day I walked into Berkeley and into the lab I was able to do research. The course requirements for the Ph.D. at that time were partially met by what I'd done in undergraduate school in physics and physical chemistry and math so I had comparatively few course requirements. All I had to do was do the research and take the examinations for the Ph.D. It was easy. I did it in two years and I'm proud to be a Berkeley Ph.D.

BSP: Right, right. Were you interested in research?

NB: Oh, yeah. That's all I was interested in.

BSP: Even when you were in the medical school –

NB: Oh, yes.

BSP: In your internship, and residency you were interested in doing something – discovering something new?

NB: In the family history it is said that my father, who was a physician, wanted to do research. He had an opportunity. He didn't take it because he had to make a living. That's the family legend. So, I was – my father died before I was seven so I guess my family looked upon me as keeping in my father's tradition.

BSP: Could you say a little bit about your family background and, you know, your genealogy goes back to where your ancestors coming from Europe.

NB: My – the Berlin's came to this country, I happen to know, in 1899. My father was about 10 or 11. They came actually from London, although my father was born in Moscow. My mother's family came here about 1890. They came from the Ukraine. My father was one of three brothers. He went to medical school; both his brothers went to law school. My mother had a brother who went to the architectural school at Columbia. There was formal education in my family.

BSP: So it's fair to say –

NB: My mother may not have finished high school. She played the piano well. She was an avid reader of the New York Times and more self-educated than anything else. My father I never really knew.

BSP: Right. So considering your family background it's not surprising for you to go to graduate school to get the Ph.D. Is it quite common for the medical students to pursue an MD/Ph.D. course?

NB: No. It's very rare. So here, at NIH, certainly by the '80s, by the late '70s – middle '70s if you look at the NIH fact book you will find that about 10% of the MDs also have a Ph.D.

BSP: I see.

NB: NIH actually set up an MD/Ph.D. program.

BSP: Right. Jumping to that area, were you involved in implementing that –

NB: No, no, no. That was in the National Institute of General Medical Sciences. I was involved in the periphery of that when I was at Northwestern University.

BSP: I see.

NB: It's not a program I thought highly of anyway.

BSP: Well, going back to your Berkeley years and after getting your Ph.D. you served as an instructor and teaching undergraduates?

NB: No, no. Instructor was a title.

BSP: Oh, I see. So, were you doing your own research at the time?

NB: Yes.

BSP: I see. And at some point you went to –

NB: England.

BSP: England.

NB: To the National Institute of Medical Research, better known in the academic community as Mill Hill. I went to study biochemistry there.

BSP: Was there any particular reason for you to choose that place as compared with other European cities or other –

NB: Yes. I knew the field I wanted to study was porphyrin metabolism. There were three laboratories in the world that were English speaking that I knew of, one was in Minneapolis, Minnesota headed by Cecil Watson and associate Sam Schwartz. I knew Cec Watson. One was at Columbia with Shemin and Rittenberg . Shemin eventually became my deputy at Northwestern and the other was in England at Mill Hill. I worked with a man named Albert Neuberger. I had met him when he came to Berkeley to give a visit as a visiting professor, you know the short term visiting professor. He was the one that was the closest to what I wanted to do. Cecil Watson I would have been in the department of Medicine and I didn't want to be in a department of medicine. Shemin and Rittenberg were at Columbia University in New York and I didn't want to be in New York City and the opportunity to go abroad and I got engaged about the time I got a fellowship so I had a honeymoon abroad in a sense. Everything worked right. It was the best lab of all the three for me to go to.

BSP: You had a special fellowship from the Heart Institute?

NB: Yes, yes. Was your question you wanted to know why this special?

BSP: Right.

NB: I think it's a title that's disappeared. There were only five the year I was awarded as best I can remember, and it was special in those days it was a pre-doctoral, a post-doctoral, and the special was essentially a sabbatical.

BSP: Oh, I see. So, it's not in the categories of post-doctoral or –

NB: It is in that – they had to give it some title and I don't know the origins of the title and I presume that it's now long since no longer used.

BSP: Is there any particular reason for you to apply for the Heart Institute's fellowship?

NB: I think what you actually did was apply to the NIH and they assigned it to an institute. Why it got to the Heart Institute I just don't know.

BSP: I see. What was your obligation to the Heart Institute?

NB: Nothing

BSP: Just produce –

NB: Nothing. My obligation was just to do research.

BSP: Do research, that's fantastic. And how many years did you stay there.

NB: I got called home about – after I'd been there about 10 months to join the Navy. I was drafted and then I passed a physical examination.

BSP: This time.

NB: I will also tell you, somewhat earlier, I think before I went abroad, I applied for a commission in the Public Health Service and they turned me down.

BSP: Oh?

NB: I always told Bo Mider – it's a name you may not know. I says, "Bo I didn't pass the professional exam" and he said, "No Nat, no Nat ,you just didn't pass the physical."

BSP: So you didn't pass the physical, the Public Health?

NB: The Public – what they had discovered – Annie Rosenberg was the Assistant Secretary of Defense for Personnel. She had come out of Macy's, I think, in New York where she was a major in their personnel department and she discovered there were about 15,000 men you had training like me during the war who didn't pay back and so the physical requirements were virtually dropped. Although when I was called up the Navy sent me to have a physical exam before I could come on active duty and I think the report was, "This officer should not be called to active duty unless he has a subtotal gastrectomy," which I refused. But I was still called up and the irony is that many years later, when I was a Naval reservist here, I got a note, "Fit for sea duty."

BSP: Could you tell me again?

NB: I was fit for sea duty.

BSP: Oh.

NB: So, that's the irony of physical examinations, qualifications, what you can do. They said I was able to go to sea.

BSP: Do you remember what year you joined the Navy?

NB: 1954.

BSP: '54. Okay, so in '53 you're still in –

NB: In England.

BSP: In England. Just sidetrack, in 1953 Watson and Crick discovered the double helix.

NB: What was that?

BSP: Watson and Crick, James Watson and –

NB: I was in England at the same time.

BSP: Right so that's why I'm asking now, could you describe if you remember anything, could you say something about excitement or anything...news?

NB: No. If it...I can remember very little of the discussion. At Mill Hill in the morning the coffee cart used to go around. At lunch on the top floor, we had a cafeteria. There was no way you could eat unless you brown bagged it, except in the cafeteria and most of the staff ate in the cafeteria. After you had lunch with both the technicians, the senior staff and all, there were two rooms, one on the right and one on the left. The technicians went to this room, and the doctoral people went to the left room and that was the coffee room. And I can't remember any discussion either at lunch or in the coffee room about Watson and Crick. I just don't remember.

BSP: So, when was the first time you heard about their discovery?

NB: After I came home. When I was in the Navy I read their book.

BSP: Read?

NB: And it was quite – you know, I knew I had to read it. It was a little thin book. *The Double Helix*, I think they called it.

BSP: Oh, I see, yeah.

NB: Subsequently Watson was on a number of our boards here and I got to know him, but not well.

BSP: Crick through – you know David Davies who is also from England was a close friend of Francis Crick and, according to record, Crick came to NIH to give a talk.

NB: The auditorium was absolutely filled. I was there.

BSP: So that would have been in what year?

NB: It would have to be in '57 or '58.

BSP: Right.

NB: And if you get the little brochures – I don't know if they gave one at the NIH lectures or not, and his name may be on the list of all those who has given the – it was too early – not the Mider Lecture, it was internal. It was just a simple NIH lecture. Later we created the Mider lectureships.

BSP: Was the term “molecular biology” quite commonplace at the time?

NB: No.

BSP: Rather biophysics or biochemistry?

NB: Biophysics was because in Berkeley while my degree was in medical physics there was a comparable degree in biophysics, which really was not open to the non-physicians. Not open to them, maybe formally or informally, but biophysics was a common term when I was in school, it was a known term.

BSP: Okay, let's get back to your navy years.

NB: Okay, sure.

BSP: Do you – did you something memorable there –

NB: Yes.

BSP: Was it in terms of research or other things? Could you comment on that?

NB: I wore the Navy uniform, but I didn't – I wasn't at the Department of Defense. The Department of Defense had an agency called the Armed Forces Special Weapons Project. Special weapons in those days was big bombs and I was assigned to that. I was assigned to the Analysis Branch of the Effects Division of the headquarters. We had about 10 or 11 men, both enlisted men, who were scientists, and officers. I like to point out that I shared a room about this size with an Army private. I was a Navy Lieutenant Commander. That man in private life was Dr. DiMaggio, assistant professor of engineering at Columbia, and had been valedictorian of his class at the engineering school. Rank did not come between us. There was another man who was a graduate student in mathematics, John Canoe in the University of Chicago. I think he was a Seaman Second Class. That's almost the bottom of the Navy ranks.

BSP: So, what was your daily duties?

NB: We had no assigned duties. That section had no specific mission. We responded to requests from outside, and I can give you one or two small examples. We were the editors, or the peer reviewers, of a book called *Effective Atomic Weapons*, now I think *Nuclear Weapons*. I read every page. The man who headed the section was a Navy Commander of the academy at MIT. When I asked him what I



should do he said, “You’ll make your own program.” DiMaggio and I did a survey and amongst other things, we wrote a paper. Never finished – we published it in the military literature and it’s occasionally referred to. *A Theory – A Study of a Theory of Shortening of Life Span by Ionizing Radiation*. Then one day, across my desk, I get a manuscript to review. It had been prepared by a contractor to the agency that –as I was reviewing it and making comments all along the line I said, “Roger this –” It was Roger Payne [spelled phonetically] was my chief. I said, “Roger, it’s not very good” and he said, “Nat, you write it’ and I did. It was for a classified handbook. Later I published it in the Armed Forces Medical Journal and this was *Military Aspects of the Biological Effects of Radiation*.

One of the other things I was a major figure in planning an emergency medical team for the Pacific test operations. The previous year or two we set off a big bomb and radiated the Marshall Islands. We were unprepared to deal with exposure from fall out. So I setup an emergency medical team and I’ll give you one more vignette or two. One day one of the quartermaster Colonels says, “Dr. Berlin would you look at a set of plans?” These were architectural plans. You know, I can read them, you know, blueprints. This was for the – do you know what the word deploy means? D-E-P-L-O-Y? Deploy.

BSP: Yes.

NB: You know I don’t know I’ve learnt a few military terms for deployment of atomic weapon at a municipal airport and it was a weapon that could be – I knew that the physics of the weapon was such that it couldn’t go critical accidentally but it could explode because of the high explosives in it. And if it exploded it would scatter plutonium, uranium or whatever it is on the countryside and I said, “You can’t do it.” So, they took me in to see the General and I told him. Then they took me to brief several of the Joints Chiefs – not the Joint Chiefs themselves, but their staffs. And then this stimulated the headquarters to sponsor some research at Rochester and the major problem is if you – a fallout, transuranic elements, how do they get transported to the surface to man? And I developed some theory for calculating on measuring the effects. So, that’s what I did.

BSP: Oh, I see.

NB: And then one day somebody appears before my desk and says, “Dr. Berlin how much radiation does it take to kill a man?” I said, “We don’t know.” He repeats the questions. I said, “We don’t know.” He says, “If you don’t give me a number I’ll go get it from somebody else.” So I gave him the standard number which you have to – I gave him a number of the qualifications and he invited me down to his unit which is a weapons planning unit and I had an opportunity to see plans from here to about twice the size – the height of this wall of maps – this is how we’re going to strike Russia. That’s what I’ve been exposed to. I’ve been out to

weapons depot. I've been to Los Alamos on a number of occasions while I was in the Navy. I enjoyed the Navy.

BSP: Oh, I see. Looking back does your Navy experiences have any influences upon your years at NIH in terms of running an organization or –

NB: Yeah.

BSP: – or doing something useful for the country? You know, it's having a big picture just out of academia and having a little military experience coming to a federal institute. Do you have any connection between the military and the –

NB: As I tried to point out to you, within the Navy I was – at the Armed Forces Special Weapons Project, the officers were highly selected. Within that I was within a group that was science oriented. So I was not really out of science.

BSP: That was my impression.

NB: Yeah, and I learned a lot about – no, I learned to collaborate. I sat on a board headed by an Admiral, a joint board on future storage. The Admiral used to point down the table at me he – there were about 8 or 9 of us on the board – he'd say, "Doc what do you think?" I can't remember what the subjects were, but I wouldn't tell you anyway if I remembered. I learned to bring people together, senior leadership in collaboration, and try to put a big picture on what you're doing. Now this maybe giving myself too much credit.

BSP: But I think...

NB: I also learned one other thing. The first man to come into my lab when I came here had already been at NIH. We were beginning to organize the inter-relationships between the senior investigators and the clinical associates. He came with Gordon Zubrod. He hadn't found a preceptor in his first six months or five months here and Gordon Zubrod asked me to interview him and I did. One of the things I asked – what was his interest? What did he want to do? He made a strong case that he wanted to study an aspect of liver metabolism and liver disease, hepatic encephalopathy. I had no experience in that field and I wasn't going to take my lab in that direction and he kept insisting and finally I said to him, "Dave if I were in uniform how many stripes would I have?" He gave me one more. "How many do you have?" Which led me to propose to him that on the company time he would work in the lab along the directions that I was setting for my lab and whatever he wanted to do in the other field, liver disease, he did. He writes that I ordered him into hematology.

BSP: I see.

NB: So, I don't know what – if he hadn't agreed on my terms he wouldn't have worked in my lab that's all. And I recognized – he recognized, I guess, or I recognized his rank. So the rank I had was head of the service, a senior investigator not a clinical associate. So, I pulled rank. So I thought in a general way.

BSP: Right, very interesting in the military having a, sort of, academic scientists working together –

NB: And I must tell you that when I came into the Navy I got – shortly after I was in the Navy I was stationed at the Oak Knoll Naval Hospital and they were figuring out what to do with me. There were two competing commands – groups. The Surgeon General's advisor on research wanted me to stay at Berkeley at the Oak Knoll Naval Hospital and serve as a bridge essentially to the campus of Berkeley. There was a group in the Surgeon General's office needed to fill that billet and I filled it. When I got to the Washington area the Navy Commander in charge of radiation problems at the Navy medical corps asked me if I would go across the river to get interviewed. I was interviewed by an Air Force Colonel. I had a clearance from the Atomic Energy Commission at that time from my Berkeley days and Colonel Lay says "I can tell you a little bit about what we're doing I know you have a clearance" and nobody ever believes this he says, "Dr. Berlin would you be willing to come to work with us?" My response was, "I will do what I am asked to do." He said one other thing to me, "Would your wife be willing to move to Washington?" I said, "At least the right now." The last thing he said, "Dr. Berlin don't come to work – when you get to Washington don't sign in – don't come to work until you're settled at home." Nobody believes that, but that's a fact. Now those are the things that drove my thinking from my Navy experience, working in a large organization that had a hierarchy and let's leave it at that.

BSP: Right, so you came to NIH –

NB: Yes.

BSP: NIH in 1956 and you mentioned in another interview that you already got to know Bo Mider.

NB: Yeah. Bo Mider offered me a job in December 1952 and I turned him down and I went to England.

BSP: So you came here just to renew that offer?

NB: I walked in December of – either January – it must have been January '55 I walked into Mider's office and he told me a little bit about some research. You didn't know him. I knew him well. He was a man of few words, mostly direct,

and he said, “Nat when are you coming to work for us?” I said, “The day I got out of the Navy.” That was his offer of a job and my acceptance.

BSP: Did you consider any other options –

NB: No.

BSP: Not going back to Berkeley?

NB: John Lawrence wanted me to come back. John Lawrence was offering – said he would make me an assistant professor. He’d been saying that for a couple of years. He never did it and I know indirectly that the chairman of the physics department was willing to make me that appointment and John didn’t send it up and I wasn’t going to stay at Berkeley without it.

BSP: I see and is there any particular reason for you to choose NCI as opposed to other Institutes?

NB: Leon Miller was a biochemist whom I knew at Rochester and when I was casting about for where I might want to be I talked to Leon. He suggested that a friend of his from Rochester come down to NIH and that was Bo Mider. I wrote Bo. Bo asked me to come here and I was interviewed, as I said, and he offered me a job. I told him I’d just gotten a fellowship. He said, “We’ll send you to England as a commissioned officer.” I said, “I’d take the fellowship.” And that was a very good decision on my part.

BSP: Right. So did you know Gordon Zubrod then?

NB: No. I met Gordon early in ’56. He called me up – I was living here – he called me up and asked me to have lunch. He was then Chief of the General Medicine Branch, probably already the Clinical Director, and he offered me the metabolism service and I took it.

BSP: Was the metabolism service just created or had a long history before you came?

NB: It did not have a long history. It largely reflected Bo Mider’s scientific interests.

BSP: Oh, I see.

NB: There were four people there, Don Tschudy, John Fahey, Jesse Steinfeld, and[?] in one way or another they all represented Bo’s interest. They offered me the job. Metabolism was essentially a euphemism for human physiology and biochemistry.

BSP: Right. How is it different from Jesse Greenstein’s biochemistry?

NB: Jesse Greenstein had a pure biochemistry lab. It had nothing to with man. When I came to work here I met Jessie. I was introduced to him as a new member of the staff. He said something derogatory about physicians and their research and I said, "Dr. Greenstein I'm a Berkeley Ph.D." He was a Berkeley Ph.D and that ended that discussion.

BSP: [laugh]

NB: And Tom Waldman and Sherman Weissman came to my lab, because they had originally begun to make some arrangements with Jesse Greenstein and that fell through and they came to me.

BSP: So, before coming to NCI do you remember any prominent scientist's names? You know like Jesse Greenstein was famous at the time or others?

NB: Freudenberg and the environmental cost of [?] which I had nothing to do with. Jay White was reasonably well known. His brother was Abe White at Einstein. Grovestine left. Alton Meister was still here. He went to be chairman of biochemistry at Cornell.

BSP: Right, so it's a fairly good group?

NB: Yes.

BSP: Could you comment on the reputation of NIH, in general, as a scientific institution among the periods in academia? Was it well regarded or just one of the government agencies? Could you – when you –

NB: It was – Henry Kaplan who had contact with NIH – was professor of radiology at Stanford. My wife was a clerical – a secretary. Henry and I were both members of the local chapter of the Society for Experimental Medicine in San Francisco. Henry Kaplan did his best to discourage me from coming here. I did not take his advice.

BSP: So there's a certain amount of prejudice against NIH –

NB: NIH...boy it's hard for me to say. NIH did not have the cachet that Berkeley or Stanford had – particularly Berkeley.

BSP: Now it's different.

NB: Yeah. Now it's Mecca.

BSP: Right. I'm interested in how it's changed over time.

NB: I can't give you – I can tell you what Henry Kaplan said, “Don't go to the Cancer Institute.”

BSP: Oh. Is it particularly against Cancer or particularly in general?

NB: His impression of me and the Cancer Institute and science in general.

BSP: I see.

NB: And within NIH, at that time, the premier institutes were Arthritis and Heart. Cancer was not.

BSP: Was that the general impression among the scientists here or is it looking back?

NB: I don't think you'd get many people to acknowledge it, but we were not as highly regarded in the academic community within NIH and in the universities. I think I helped change that.

BSP: Yes, I want to follow that a little later. Going back to Jesse Greenstein's comment, the derogatory comment on the physicians, just M.D.'s or others?

NB: As scientists?

BSP: Yes, as scientists. After coming to NCI did you understand why he said that or did you disagree with him or you –

NB: There are elements of truth in what he says. Physicians were not necessarily good investigators. I said there were elements of truth. Particularly – what you have to recall – no you don't have to recall. In the medical community, in the medical schools particularly, the Ph.D.'s looked down their nose at the M.D.'s – they simply made too much money, our salaries were too high and we didn't do good research. That was a common broad based holding, which again...had elements of truth in it, but couldn't – they couldn't sustain that for a long time in terms of – say from 1950 to 1960 to 1970 or even to 1980 and the '90s.

BSP: Right that's what I'm trying to see that – to trace the changes and what's the important factors and let's go back to NCI's intramural program when you came here. You are in the Metabolism Service within the General Medicine Branch –

NB: Right.

BSP: The General Medicine Branch is in the Institute. Are there any other branches in the laboratories? Could you describe the general layout?

NB: Well, the word “branch” was used to describe the title of a clinical unit. The basic science units were called labs. So, there was a Surgery Branch, an Endocrinology Branch...and I can’t remember the remainder.

BSP: And the basic science branches...

NB: There was a Biochemistry of Biology and Pathology – the Laboratory of Pathology was both a laboratory within the Cancer Institute, as a research laboratory the Cancer Institute. It was the pathological anatomy service of the hospital so they did the hospital pathology and that was – they had problems with me when I became the scientific director but I’ll get back to that possibly.

BSP: So, the clinical unit and the scientific unit were all in the Clinical Center?

NB: No, no. Building 6 housed biochemistry and biology. Surgery of course was in the Clinical Center, my unit was in the Clinical Center. There was – Physiology was in the Clinical Center. That was the lab that I’d forgotten about. Again there was that division of clinical people in the Clinical Center, basic science building in Building 6. You know, in a broad sense.

BSP: So, in the sense of – that was there any certainty of interactions between the basic science part and the clinical people?

NB: Comparitvely little. John Fahey got some help from Elbert Peterson in the chromatography. And Don Watkin got some help from Jesse Greenstein’s people.

NB: So, how much help there was from one to another – I knew that it existed, there was not a great deal. There was a gulf. There was really a gulf.

BSP: Right. How about within the clinical units in the Clinical Center? Were there any flow of information and, you know, that the basic design of the Clinical Center is to promote the collaboration between the science and the clinical side.

NB: What we had – first of all I will say the Clinical Director and Gordon Zubrod coordinated that until I became the Clinical Director and we had Friday mornings at 11 o’clock we had the grand rounds in which it was expected that all the clinical people would attend and we rotated subject, departments, etcetera. The other thing is Zubrod made rounds on all the services and I eventually did and once a month when he was the Clinical Director he reviewed all the autopsies and I kept that practice going. So, a lot of it flowed through me, a lot of it flowed through a combined grand rounds and for NIH as a whole we had combined clinical staff conferences where an institute put on a program for all of NIH.

BSP: Bo Mider was the Scientific Director?

NB: When I came here, yes.

BSP: And Zubrod became the Scientific Director after him?

NB: Bo left, yes.

BSP: And as the Scientific Director these people were in charge of both the basic science and the clinical –

NB: Yes.

BSP: And at some point there was separations of divisions?

NB: In the mid 1960's Ken Endicott, who was the Director of the Cancer Institute, created a study group headed by Gordon Zubrod, and I think the basic intent was – well, let's go back. The Cancer Institute put its eggs in three baskets. It put a very big egg in cancer chemotherapy, a very big egg in cancer virology and it didn't know what to do with the rest of us. So the intent or the effect of that study group that Gordon put together was to give him an opportunity to choose which one of the laboratory branches in the institute would come into his Division of Cancer Chemotherapy later to become the cancer treatment, and the same thing was given to Rauscher and then the rest was left to be called general labs and clinics with no specific mission. Eugene Van Scott got that originally. I thought I was going to get it and I will tell you frankly that the basic science chiefs, I learned many years later, had told Ken Endicott that they didn't want me and one of them later came to me and said I made a mistake, because they got me. They thought I was too clinical and I wasn't and they didn't realize that they had a real friend in – well they didn't accept me for what I was so I eventually became the Director. Bo Mider's title when he moved to Building 1 was Associate Director, I think, for General Laboratories and Clinics and that's the title that was evolved – or given to the third division, the third intramural division. Now when Bo was the Scientific Director he did not recognize the others as scientific directors.

NB: And I was the only one that he was willing to recognize as a Scientific Director initially.

BSP: That's really interesting. Could you describe the structure of your division? Was it composed of clinical side and the basic side?

NB: Yes.

BSP: Was it about half and half?

NB: I will show you this afternoon the picture of the lab branch chiefs. There were about 12 or 13 of them, about half basic laboratory of molecular biology biochemistry, half in pathophysiology and physiology. On the clinical side



initially endocrinology, surgery. But when I became the Clinical Director the four sections of general medicine, dermatology, and metabolism, chemotherapy, and clinical pharmacology each became branches. They were all – clinical pharmacology did not report to me nor did chemotherapy, but dermatology, endocrinology, surgery, my own, they didn't report to me directly, but they did because I was the Clinical Director. They couldn't do anything clinically without my implicit approval and actually I had a minor title in Gordon Zubrod's Associate Scientific Director for something, which I never used. The beauty of it all is for me and Zubrod together. Vince DeVita once told me, "Nat when you and Gordon were both here never was there a more powerful duo in the Cancer Institute." So, titles did not mean much at least it didn't mean much to me. The flow of authority I knew what I had and what I didn't have. I didn't need it.

BSP: I guess there is a very important moment for the history of the NCI's intramural program, because it shook up the previous structure, which is the scientific.

NB: Well they gave – in contrast to the other institutes it gave two – the general laboratories and clinics turned out to be the largest of the units. In some respects, intramurally, it had the least money for outside activities and contract supported. It was a recognition, as I said, we were going to cure cancer with drugs or we were going to prevent cancer with viruses by finding a viral etiology and developing some virally derived preventive. We have not succeeded in either. On the other hand, it is generally acknowledged that cancer biology, both in my division and nationally and internationally, has flourished and so this afternoon I will point out, in a nice way, I hope in a nice way, that by leaving – by having a division without that specific mission was what I said that all biology is cancer biology.

BSP: Oh, yes.

NB: And even that worm, whatever, the *C. elegans*, contributed to cancer biology.

BSP: There is no doubt about it.

NB: And that was a fundamental credo of mine. I say ethos this afternoon. And so when Ira Pastan came to work he asked me, "Nat do you have any" – he sort of asked me if I had any indications of my own to what I expected him to do in terms of details scientifically and I said, "No." And then Ira pointed – said to me, "Nat, what if I work on an artificial heart valve?" And I said, "it better be good."

BSP: So, you have a complete confidence in the scientists like Ira Pastan?

NB: Oh, sure. They were better scientists than I.

BSP: That is something recurring among the well known Scientific Directors like DeWitt Stetten, James Shannon, of course was the Scientific Director for the

Heart Institute, and some others who really – who did their job by picking some promising talents and then let them do whatever they want to do and just guide, not lead, guide their research by eliminating other administrative duties and other concerns. Is that the same philosophy you adhere to?

NB: Yes.

BSP: Is it particularly an NIH philosophy?

NB: NIH is different. I've worked at Mill Hill and I've worked in Australia at the Walter and Eliza Hall and they are both major, much smaller, biomedical research institutions. Mill Hill had a very strong director when I was there, Sir Charles Harrington, but his department had truly distinguished scientists and it was a training ground for British science. The Walter and Eliza Hall had a great director Gustav Nossal and I don't know – Gus also played a major role in their immunology research but he also had a half a dozen section heads, division heads, call it what you will, who were highly successful scientifically. Gus was supportive – I don't think Gus ever told them exactly what to do or how to do it. I think he viewed it as his role to see that they had the resources they needed to represent the institute within Australia – the Australian government, the Australian public. And he did. Shannon represented us to the Congress.

BSP: I want now talk to the role of scientific directors in running the program and the change in the program and wisely shifting the focus. I want to go to the period in the 1960s and up to the early '70s, the period when NCI was really changing. When the NCI intramural program was changed at the time, who was the most influential? Did the institute director the person who made the final decision or it was up to the scientific directors? What were the mechanics involved in the change?

NB: The institute director was the institute director. NIH had a scientific director, Bo Mider, or Bob Berliner in my time. The scientific directors of all of NIH used to meet twice a month, Wednesdays, the first and third Wednesdays. We were a very collegiate group. In some degree, it depends on who you're talking to, the institute directors lost a good bit of their control over the intramural program because the scientific directors had direct access to the Building 1 Scientific Director. Berger [?] got angry at me once when he said I bypassed him. Ken Endicott fretted under it. But we all understood when I selected Steve Rosenberg to be Chief of Surgery, the first person I went to speak to was Bob Berliner. When I brought him to [?] he was the first person I spoke to because he had to approve the appointment. It was all up to Bob Berliner. Ken Endicott was a good director. Furthermore, you have to recognize, at least in retrospect recognize, in terms of his missions – the orientation as I said, treatment and virology – my division was unimportant. I couldn't get up and say to the National Cancer Advisory Board, "We're doing good biology." When I once went to them with some of my thoughts about creating a laboratory of theoretical biology, Benno

Schmidt questioned me, "What is theoretical biology? Why do you even want a laboratory of theoretical biology?" But he didn't say no. They questioned, they didn't understand it. So in a sense I was largely unaccountable. Accountable to Ken, yes, accountable to whoever was the director at NIH and more particularly the deputy director – the deputy intramural director. During my clinical director years, Jack Masur around the hospital. So I had a multiplicity of people that I was held accountable for. Now the clinical directors only met once a month. We were not as effective as a group as the scientific directors.

BSP: Is there any possible reason for that?

NB: We didn't have – Jack Masur chaired that group. Bo Mider came regularly. The commonality was the operation of the Clinical Center as a hospital, and that we had a medical board, which I sat on for about a decade. But they didn't hold promotions, they didn't review promotions, they didn't review what we were doing, in a sense. Amongst issues we once discussed was "what procedures require a written consent?"

BSP: I see, it's not specifically related to the program.

NB: They were hospital – right – clinical care issues. Our relationships with the nursing service, mine were fair to good. My relations with clinical pathology, particularly the hematology department, were bad. Because I held the power, they didn't.

BSP: So it's – let me clarify your division of general laboratories. Some groups in the Clinical Center – some labs still in the Building 6 –

NB: And then in Building 37.

BSP: Building 37. In the late '60s and early '70s you also had a round with the physicians in the Clinical Center?

NB: Yes. All the time I was the clinical director I made rounds regularly.

BSP: I see. The Clinical Center has a clinical director's medical board meeting, and scientific directors have their own meetings and they have scientific directors' meeting. You were kind of in an interesting position.

NB: For a long time I was in both.

BSP: In both is unique. Could you comment on looking at both sides, in terms of integrating clinical programs with basic sciences or in terms of what is now very popular terms such as translational medicine?

NB: I don't know whether – I don't like that term and I don't know whether they derived it from transcription and translation and the DNA sequence. You took whatever it was that the DNA – where there was knowledge and they eventually ended up with a messenger, and that was translation. I did a translation when I was – with my hands – when I was a Fogarty fellow in Australia. With few exceptions of the scientific directors were physicians. John Eberhart in mental health was not, and I don't know whether Degrossi [?] was in the Dental Institute – he was a dentist, a physician or what. I think our job as a scientific director was to represent our community, certainly to hold the appointments in our division, be responsible for a lot of the budget, the clinical director was responsible for patient care. We had a scientific director, which I think eventually became an executive committee, of the cancer institute where we discussed very broad issues. I can't give you a good answer of how we functioned. I gave up my own personal research about 1970 about the time I moved into this building.

BSP: Yeah, it's – what strikes me about NIH history is that there are many different groups of people who make different decisions, but somehow it's working very smoothly in a coordinated way and I was just curious how that kind of coordination – the running of the Clinical Center and the running of the institute and the running of the internal program are all somehow connected .

NB: They are connected, and you have to remember Jim Shannon was a great leader.

BSP: In what sense?

NB: He was a good scientist, he was a nice man as a man, basically humble – that's all I can say. When Bo was there, Bo was a great leader but in a very different way. In the decade that Ken Endicott – almost a decade, I think Ken was a good scientist. He had a good understanding of people. He'd grown up in the public health service, did his research – actually I think he may have worked in the same lab with Kornberg at one time, and others who were interested in the disease. Zubrod was certainly a wonderful man. We didn't have, within the Cancer Institute – Rauscher and I got along, Rauscher got along very well with us. This is all intramural. We played no role – virtually no role in what Palmer Saunders and Tom King did extramurally, in terms of grants. They didn't like us very much.

BSP: Is there any reason for that?

NB: I'm getting old and I can talk. At a meeting – at a dinner, across the street at the officer's club at the retirement of one of their senior staff, you might know him quite well, Palmer Saunders got up and said something like this, and some of the intramural staff like Matt Berlin looked down their nose at us. In a sense, we didn't know what they were doing. At one time I thought they were manipulating the grants process, that they had intended to take on science that they were not prepared to do, in terms of program leaders. Now that's an arrogant view. The

other thing is, at one time, the numbers may not have been large, at one time it was fairly common that those who were stumbling in the lab could go over to work for research grants. It was an honorable place, they got their salary, I participated in that process and if somebody listens to me a few years from now they'll say, "He was an arrogant bastard." Me.

BSP: You're talking about the grants program, but what about the contracts? The intramural program – NCI has a collaborative program –

NB: This was, in large measure, if it wasn't created by Ken Endicott it was supported by him. The contractor's mechanism was not liked in the academic community, he was not liked in parts of NIH, he was heavily criticized.

BSP: The uniquely NCI programs?

NB: Did I?

BSP: The collaborate programs, the contracts program is only NCI programs or were there any others?

NB: In other institutes?

BSP: Yeah.

NB: I can't say. NCI used them in a very major way, Buettner and Bob Gallo. They were a very effective way of getting research done – you didn't need to tell somebody to write a grant. Gordon Zubrod set up, in the mid '60s, a whole plan for chemotherapy research that was largely contract-based. And on the cooperative side there were grants for the cooperative groups – I sat on the original Cancer Clinical Investigation Review Committee. I had three contract programs: one in diagnosis, one in the breast cancer task force, and one in immunology. I ran the first two, Bill Terry ran the third. We could do things that you could not have easily done with grants – mainly, put a lot of money into specific projects, and if you go to Bernie Fisher and you ask him what I did, he'll tell you about what I did for breast cancer. Or you go to some of the lung people – lung cancer screening people or the breast cancer screening people, they can tell you what I did for breast cancer screening. I set up a committee and gave it some money – saw to it that it had money, a couple million bucks a year, for cytology automation because I made the decision that the Pap test should be automated. And when Maronpot [?] brought some people to see me from Las Alamos who were developing a cell sorter I arranged for them to come give us a small seminar, to Ken Endicott, and we transferred a quarter of a million dollars from NIH to AAC to get the cell sorter started. Now do you think they could have gotten a grant to do that?

BSP: It might take a decade.

NB: Well, we recognized – I had a friend of mine here, one of colleagues from Berkeley was a good biology engineer, and we listened to their presentation and I said, "Will, is it good?" He said, "Yes." Gordon Zubrod did the same thing with IBM and it wasn't a cell sorter. I forget what they called it – a plasmapheresis machine; put some money into IBM, IBM put some money more – initially IBM put the money into it, Judson was one of their senior staff, Judson had a son who was a patient here, he got into contact with Freireich and they built that machine. Now do you think they could have gotten a grant for an idea? No.

BSP: So how were the grants reviewed?

NB: The grants or the contracts?

BSP: Oh, the contracts, sorry.

NB: Contracts were reviewed – we had contract review committees. I had about 11 in my division and they were almost all outsiders.

BSP: What is the success rate? How many were turned down?

NB: What we did is – there were two things we could do. At one time we could sole source an educational institution. And somebody at NIH didn't like that and got that stopped. I know the man who did it and I didn't like it – he and I were friends, he and his wife and I were friends. He also issued – where we didn't want to sole source or we couldn't sole source, we issued a request for proposals which would describe the science. The proposal would come in and we would have the review committee review the proposals and rank them and the top ranked got funded, and they had funded one or two or three. Actually, when I was at Northwestern, we submitted – we responded to a request for proposal to create a pain study. We were successful. Could we have done it through a grant? No. Not likely.

BSP: Scientific director's meting has anything to say about the management of contracts?

NB: No, almost nothing.

BSP: Almost nothing, I see.

NB: That I can remember. We'd go over housekeeping issues, we reviewed all promotions and in the Spring of the year every one of us came in with his promotion plans.

- BSP: So why was it so criticized by its primary communities and some of the intramural communities? Because it has a good intention, it has a good product and has a direction? Something that cannot be done by grants mechanism?
- NB: There are several-fold criticisms. The underlying one in the academic community was if we had \$100 million in grants and contracts they told me that we could get more research done better and cheaper if it were in the grants mechanism. They criticized the quality of the science. They resented deeply the fact that Bob Gallo had a lot of resources, or Bob Buettner had a lot of resources, which they used to do probably good research but it was – at the same time, it was financing their careers. One would hear nobody could manage that much money or that many people or that much science. And then one year I got concerned about Bob Buettner, I looked at it. The previous year he published 33 papers with the contract. Bob Berliner once told me he thought his research was good. What do you do? So there were a few people at the NIH – Leon Jacobs particularly I remember – who did their best to get us out of the contract mechanism. Since I utilized it, was happy with it, I think the NIH made a mistake. September 1974 we put on a meeting, I gave a report to the profession on the breast cancer task force. We didn't advertise it, we didn't send out notices. We had a hidden agenda. The Masur Auditorium was filled – I don't know how the word got out. The press were there. I purposefully promised one of the investigators there would be a no press room and no press conferences. I think Jane Brody or somebody else from the press castigated me for not having a press conference. Jack Masur got into the process and created a little press conference eventually. Paul Van Nevel who was here, said that was the first day he came to work and I blasted him for doing it – he told me that 25 years later. I made a commitment there would be no press conference and I was determined to keep it. It was a broadly-based report of what we were doing. I am told it was the last NIH meeting, the very last attempted – Dietert told me that about a year ago. That's what you can do when you have resources.
- BSP: Right. Now this –
- NB: I used to bring the breast cancer task force all together into here or to Williamsburg or out in San Antonio. I brought all the diagnosis contractors together for scientific presentations – I let Bill handle the immunology ones.
- BSP: I guess this brings us to the bigger context for getting a large amount of money to NIH, which is related to the National Cancer Act in 1971 –
- NB: And the bypass budget.
- BSP: Right, bypass budget –
- NB: And the president's panel, and Benno Schmidt.

BSP: Right. I'd like to talk about that after changing the tape and then taking a little break.

NB: Go ahead.

BSP: This is the second tape of Dr. Buhm Soon Park's interview with Dr. Berlin on the history of NIH intramural program. Dr. Berlin, could you continue our conversation on the subject of the National Cancer Act in 1971 and how it affected NCI programs in general?

NB: Yes. You must remember that the act followed a panel – the Panel of Consultants on the Conquest of Cancer; I think it was chaired by Josh Lederberg and Sidney Farber. The panel was created by Senator Yarborough and a godfather – I want to say the god-grandmother was Mary Lasker. I was – as we go up to the director's office, here's a photograph of Nixon signing the act, I was there then. The act required a president's cancer panel and a bypass budget. The ordinary budget process was each institute submitted a budget and then it was managed by the director of NIH and then dealt with by the Office of Management and Budget. The compromise was that the Cancer Institute would have a direct submission of its budget to the White House – mainly the Office of Management and Budget – and the compromise was the DNI's could comment on it. The net effect, we would prepare the bypass budget. My office prepared part of it Rauscher's office prepared – each of us prepared a section. I think in large measure Benno Schmidt took it wherever he took it. Then it got to the Congress – no then it got into the President's budget. I have never looked to see if there's a concordance between our bypass budget and the budget message that the President sent out in the big telephone book of the budget – I've never looked at it. I have a sneaking suspicion that the numbers are very different. The net effect, anyhow, was a very rapid increase in funding in the early '70s, and this was a relief to us in the Institute, more particularly to grants people, because in the beginning of the middle '60s we were beginning to feel budgetary pinches. That's the history.

BSP: Right. What about the other institutes?

NB: The other institutes resented this, they resented the budgetary increases. The leading budget people – I think it was a man named Finch and some apparatus in the White House made the case that the increase in the NCI did not come at the expense of the other institutes; many years later he admitted that that was not so. And if you go to Earl Laurence – do you know Earl Laurence in the Arthritis and Metabolic Institute? I think he's their executive officer. One of the pathways from the Clinical Center to the Cancer Institute when they need money was through me. We had money – well, enough.

BSP: And were you delighted about the pass of Cancer Act in 1971?

NB: Sure.



BSP: Was that the general emotion among the Cancer people? Were there any –

NB: I can't say that in the academic community there was any response. The academic community was interested in R01s and more R01s and more money for R01s. That was their interest. As I pointed out, they were not interested in support of the contracts, and even somewhat less supportive of cancer sonographs.

BSP: Could you say – after the Cancer Act in 1971 – the contract in cancer was strengthened or contract mechanism was expanded, or –

NB: I don't think it was either strengthened or expanded, it came under criticism, and again, eventually folded; almost completely destroyed. I don't think it's completely, it's still there. But a very different mechanism – very different utilization.

BSP: So you have a lot of budget. Where did you spend it? You're telling me mostly the basic research part and the general bio –

NB: Well in my division – the budgets and intramural program, we had money for – we didn't have a budget, in a sense. We had access for the diagnosis to breast and immunology. The breast cancer group, after I took it over, that task force group from about a million and a half up to eight million when I left. Kenny Painter, my administrative officer would go upstairs to see the budget office and tell them we needed money.

BSP: So, for example, the laboratory molecular biology you just created for Ira Pastan had a lot of support after 1971? Was beneficiary of the Cancer Act, is it fair to say?

NB: It's fair to say, but it isn't relevant – it really isn't relevant. The whole institute had support.

BSP: I see. It's not – one particular laboratory is not –

NB: No.

BSP: Did you have any intention or goal of expanding the basis of the cancer research with, say, molecular biology or –

NB: Yes. Molecular biology came about in two ways – there were two major thrusts, to my thinking. When Herb Silber died, I made the decision that I didn't want to keep the laboratory of biochemistry, and in the fall it was. Ed Rall was the acting. And I said, "Ed, I want to split the lab up. You come in with a plan." My basic plan was, "Ed, take all the good people and put them in one unit, put all the ordinary" – the less successful people, not ordinary, "in another unit and we'll

gradually let it wither away." Now then, new science, one of the major problems of a scientific director is how to respond to new science. In an institution and as a structure and organization and everything else. The wrong way to say it – and I'll say it – in many respects, I had to build new science out of the ashes of old resources. One day Ed Rall and I came to the conclusion that the logical way to develop modern biochemistry was to have a new laboratory of molecular biology. One day, walking across the campus, Ed Rall says to me, "Nat, we've got to do something about Ira." Well Ira became the Chief of the Laboratory and Molecular Biology. He said he wanted a small lab with 13 divisions – he got it. He expanded them under my – I don't know if he expanded them much while I was around, but he certainly did with Al Rabson and that was the Laboratory of Molecular Biology.

BSP: So the term "molecular biology", the "Laboratory of Molecular Biology" was chosen by you or –

NB: Yes.

BSP: You were thinking about theoretical biology at one point?

NB: At one time I put together a plan for the Laboratory of Theoretical Biology. I had picked out in my own mind – I never talked to him about it but it was going to have three units in it: one a nucleic acid chemistry, one a mathematical model and physiological processes and one a computational laboratory. We never did get a chief of theoretical biology. The mathematical became Jake Maizel's Laboratory of Mathematical Biology.

BSP: And the other senior investigators were chosen by Ira Pastan or chosen by you?

NB: Not by me. They had to pass me. They had – Ira had to come to me and say, "This is who I wanted."

BSP: That's very interesting because I studied the origins of another – the Laboratory of Molecular Biology at NIAMD, created by DeWitt Stetten in 1962. Stetten sort of drew the whole picture – the section chief and the lab chief and it seems like you just picked Ira Pastan.

NB: And Ira developed the lab.

BSP: So basically you were pleased with what he decided to run.

NB: You have to look at what he's accomplished and his people.

BSP: I see. So the NCI intramural program, especially the basic research program, was the beneficiary of the Cancer Act in 1971, but not particularly as a general beneficiary?

NB: It was that the whole institute was a beneficiary.

BSP: Right.

NB: I wouldn't think of it in those terms. The National Cancer Act was a means of getting us more money and we got it – the whole institute did.

BSP: In comparison with that, the divisions like the prevention and the treatment, your division was small – received a small –

NB: We had a Cancer Control Division.

BSP: Is it that the Cancer Control Division was a separate division?

NB: Yes.

BSP: Is it originated from the existing cancer programs or it just seeded from outside?

NB: The Cancer Control Division, if you go back to the National Cancer Act, they made up a special provision and put money into it, a line item appropriation for money for cancer control. The basic assumption at that time was that those of us in universities, those of us here were doing research that impacted on the ability to take care of patients but it wasn't getting out to the universities. So that became – when the act was passed Carl Baker asked Palmer Saunders, Gordon Zubrod, Dick Rauscher and I to prepare a cancer control program. I was going to handle the diagnostic treatment part, etc. It never came about. It had ineffective leadership because it really didn't understand what cancer control was or could be. The model of cancer control that existed in the past was demonstration projects – created, maybe, in the '50s tests.

BSP: So the new program was built on the old program?

NB: I don't know if John Bailer came in to run that program but it didn't last very long. I did was run the best cancer detection demonstration projects in the diagnostic program – I didn't let them get in my way.

BSP: I see. Let's get to the point of each lab. Each lab has a lab chief and senior investigators.

NB: They might have had sections too.

BSP: Yeah, sections and each PI or senior investigator have clinical associates and –

NB: That's on the clinical side.

BSP: Right, and under basic research side the research associates were?

NB: We eventually began to participate in the Research Associates Program.

BSP: So could you comment on – well let's go back to the early '60s or late '50s – how you picked the clinical associates among the pools of applicants.

NB: How they were chosen?

BSP: Yeah.

NB: They applied to an institute and they were interviewed within the institute. In the Cancer Institute, I set it up so that those who were interested in surgery were interviewed, if they wanted to be, by the surgery branch. In the metabolism service each member of the service could have one clinical associate so we interviewed every other year and I interviewed like that every other year. And the other units, they might have interviewed people that wanted to come to medicine or pharmacology and they didn't make a commitment to them to a particular investigator. They made a commitment to them. And what they would do, the applicants when they left here would rank their preferences and we would rank their preferences, and when the interviews were all over I would send up a list to the Clinical Center Education Office of a priority list and they would match. If you want a match service and tilt it towards the institution or to the applicant, it's my understanding we tilted it to the applicants.

BSP: Mmm-hmm. I see.

NB: And so I was pleased when I would get my first choice. When the surgery department had four to six applicants and we'd get – maybe five out of six were their first choices. And I have been occasionally teased later by people who said that I interviewed them and they didn't come to work for me would become very distinguished.

BSP: So the clinical associates applied to your particular institute or NIH in general?

NB: To a particular institute.

BSP: A particular institute, I see.

NB: And they indicated this was – now we would call it a roadmap. There are earlier editions of this. I don't know where they are.

BSP: Each year there is a quota for NIH to offer the clinical associate's positions, right?

NB: A quota?

BSP: A quota, the total number of clinical associates that can be appointed by the NIH and the number was divided up to...

NB: I can't tell you that it – it may have been at the Public Health Service level. It was ineffective at our level, because one of the first things I did is I went to Zubrod and I said, "Gordon, we ought to increase the number of clinical associates." Both of us went to Bo Mider. Bo said, "No." The year he left to go to Building 1 we doubled the number.

BSP: No problem at all?

NB: No. We were the largest consumers, the Cancer Institute – the largest users, I'm sorry. There may have been a quota at the Public Health Service level. If there was, I'm almost unaware of it. It was not our – as far as I was – nobody told me I couldn't double the number.

BSP: What I'm thinking is because the clinical associates are usually chosen among the top medical students and they are very useful and so that the people – it's natural to think that the institutes have a competition – want to increase the number of the clinical associates within their division and having service and also training them may have a big – just like you, double the number, but I –

NB: That didn't pervade the rest of NIH. I said that we were the largest users.

BSP: I learned from the scientific director's meetings that NCI joined the research associate program a bit late.

NB: That's right.

BSP: It started '57 but joined in '61, something like that. Was there any particular reason for that?

NB: Well, there were three classes.

BSP: Right.

NB: Clinical, research and staff. The clinical ones and the research associates were the matching program. The staff associates were not. We came into the Research Associate Program comparatively late. The research associates were not in the clinical units, they were in biochemistry, biology etc. We had residents in pathology, not clinical researchers. I'm choosing my words. I was just not prepared to open up the Research Associate Program for the biochemistry lab, for the biology lab, for the physiology lab and it wasn't, I think, almost entirely – it wasn't until Ira came in that I opened it up. The first year I selected them and then they came here and when they were ready to come onboard they interviewed in selected labs. Ira came to me and said, "Nat, I'd like to – would you be willing

- to let me interview for my own lab?" I said, "Sure." A couple of years later he said, "Nat, you may have picked better than I did."
- NB: He did all right.
- BSP: Chris Anfinsen.
- NB: I knew Chris.
- BSP: Yes he was the person behind the Research Associate Program.
- NB: The Research Associate Program, certainly in the Heart Institute.
- BSP: Right, and he had a certain vision of training.
- NB: If you look at Chris' lab he was probably the only Ph.D. in his lab.
- NB: His successor is Alan Schechter, if I'm not correct, who's an M.D.
- BSP: Right, that's true.
- NB: I think I once looked at everybody in his lab.
- BSP: So he liked the person who comes through the Research Associate Program?
- NB: Research associates.
- BSP: Yeah, and this Research Associate Program, through which some people tried to create a kind of graduate school at NIH...
- NB: Yes, we wanted to. We wanted to be able to get award degrees. We were bitterly opposed by the academic community.
- BSP: Not within NIH community?
- NB: No, we were opposed – I think it actually got up to the congressional level. The academic community – we had lots of money. We could offer graduate students what they couldn't. We could offer them freedom from writing fellowship applications, and so a few people got their degrees down at G.W. like Julius Axelrod.
- BSP: Were you involved in that movement in creating a graduate school?
- NB: No – I supported it. I was not on the – the Cancer Institute wasn't in DeWitt Stetten's orbit. I fully supported the effort. I don't know that I ever gave them tangible support in any way. I would have loved to have seen it.

BSP: Have you talked at FAES evening classes?

NB: Have I talked to them?

BSP: Yeah.

NB: Well I've lectured at them once or twice, not often. There was a program that I was fully supportive of.

BSP: I see. Was it useful?

NB: Of course.

BSP: So it's – so teaching and research?

NB: You have to understand, we were a research institute. The leadership came from academia. We knew what it took to make a great institution, and a great institution requires a continual infusion of young people. You have to offer young people something. The something that you offer those that don't have an M.D. is a Ph.D. That is their ticket to advancement in the academic community. And what we did – one of the other things both Ed, Don and I did principally is create the Summer Medical Student Program, because when the draft went off we wanted to bring medical students here and expose them. Eventually the Howard Hughes people did it. Don Fredrickson, when he was director of the Hughes pointed out to me that was the model that he used.

BSP: So there was a continuing effort to bring in bright students –

NB: Yes.

BSP: With researchers to make them the researchers.

NB: And the Howard Hughes Institute did it when the doctor draft went off, but I don't know how many came here as medical students under the Howard Hughes program and eventually came back to work in the intramural staff. I just don't know.

BSP: Somehow the doctor draft, which was started in 1950, just pushed the medical students to NIH, it seems.

NB: They didn't want to go to Vietnam if they could avoid it and they all admit it.

BSP: Right.

NB: And anyone who doesn't admit it is less than candid. The fact is that many of them came here and have become eminently successful internally: DeVita in the Cancer Institute, Tom Waldmann in the Cancer Institute, Dick Hodes, who runs an institute.

BSP: Gallo was?

NB: Gallo.

BSP: And Mike Gottesman...

NB: You'll see it in here. It was the best recruiting mechanism ever devised.

BSP: Could you comment on the impact of the clinical associates on general American medicine?

NB: I think I did earlier. I don't know of any other program that's had a greater impact on American medicine. If you look at the leadership of the '70s and '80s, the '90s the impact is already gone, or at least in this century it's gone because there were none coming out. Whether it was in industry with Roy Vagelos or the director of the Dana-Farber, the dean at Northwestern. You know, I could put name after name after name but NIH has never really put one together – I did it for a single unit. Oh, I can't say anymore. I wouldn't – the chairman of surgery – the chief of surgery at – no, he came on another process. The chief of surgery at Emory, I think he's Don – the dean at Connecticut, a president – an interim president at Hopkins.

BSP: It's interesting the clinical associates or research associates or staff associates came out of medical schools as among the top students and they had experience – research experiences and there were clinical experiences at NIH. And then later on they had really good careers which had a great impact upon American medicine and especially clinical research area, or what is called physician scientists – that category. I'm interested in what NIH specifically offered them. They came out of medical schools as top students and probably they could have good careers, reasonably good careers, but NIH offered something. Could you describe what NIH offered them, the way they think and the way they researched?

NB: What it offered them?

BSP: Yeah. Or simply put them together.

NB: It offered them an opportunity to do research. It was unfettered. They didn't have to write a grant, and they wrote a one page or so annual report. I collected the bibliography of the service once a year and that was my report to the director, "This is what we published." Needless to say, it wasn't inconsequential. We



offered them an opportunity, and in the early days we offered them – they came here for two years obligated and many of them we offered a third year and many stayed. Some stayed for four and many stayed permanently – Tony Fauci. Did I mention Waldmann and Hodes? That’s what we offered them.

BSP: After having spent three – two to three years at NIH some of them just decided to stay here or some others went back to academia or other sectors of the society and then somehow some of them tried to recreate the atmosphere that they had at NIH, is that accurate?

NB: I don’t know. I’ve never looked at it.

BSP: The clinical associate and other associate programs, is it true that they – that program elevated the reputation of NIH?

NB: Enormously.

BSP: Enormously.

NB: Because we took in good people and we sent them back – 90% went back, whatever the number is. And as I point out here from the metabolism service, from the beginning to the end of the time I left we had about – until the doctor draft went off – it went off and I went off, in somewhere in the order of 60 amongst the draftees was of my own service was a Nobel Laureate, a Medal of Science winner, at least three members of the National Academy, 18 members – do you know the Society the Old Turks – the Association of the American Physicians? We only take in about 40 a year. Or the American Society of the Clinical Investigation of – used to take in only 40 or 50, now takes in 80 – took in 22 of them. Nobody did anything – no program that has been as successful as that one in building that kind of clinical investigators and there’s been nothing else that’s been as successful building the national cadre of medical oncologists.

BSP: So what happened after the draft ceased in 1973?

NB: They weren’t recruiting at the same level of academic excellence. They just went and I have no idea, because I wasn’t here to evaluate the people who came here and went. The one thing is there was very little traffic, with a few exceptions, from abroad, certainly on the clinical side. I had one or two. We had no women. We were all Americans, no blacks, no minorities – religious minorities yes, ethnic minorities no. Over the years in my own way, can you excuse me, you walk through the clinical – do you know what the tower of Babel is? Okay. So I walked into a lab yesterday afternoon and the night shift, very good looking young girl sitting there, I start to speak to her. I suddenly realize she’s Swedish, she can’t give me an answer. That was not there – now there were a few people who brought in a lot of Japanese and exploited them – pure plain exploitation. And I once was a visiting dignitary in Japan and I met somebody, he said, “I’ve

met you,” and he pulls out a phone book and shows me an NIH phone book. So it has changed. I don’t think – I don’t know that they attract very substantial – in an organized way there is no program that’s bringing in people to get into a matching program to begin to come in at the entry point to a clinical research career. That doesn’t exist at NIH, and yesterday I met one man in the Cancer Institute – nothing would do more to rejuvenate the NIH intramural program than to have a war and a draft and a doctor draft.

BSP: In your article it seems like you think or you propose the clinical associate program as a kind of model of training physician scientists or clinical researchers, but without the doctor draft how can it be possible? How can we get the people to come to a place like NIH or any other institute, or create such a critical mass of good students doing science?

NB: The first thing you have to do, which Don Fredrickson and Ed Rall and I did when the doctor draft went off and our egos were deflated to the bottom, we brought about 20 medical students here, created a structured interview. We never analyzed the data, that was our fault. What I think you have to do is what I pointed out in one of my little brief articles, not widely quoted, not well known – what are the deterrents? And then you’ve got to go ask the young people what do they want? What do they want to see as the opportunities for a future? Did I tell you the anecdote about when I was in Chicago when I was teaching and had a group of medical students one afternoon a week for about a month – one girl had come from Michigan, did I tell you that?

BSP: No.

NB: I tried to learn something about the five that I took and I asked her where did she go to school in Michigan. “What did you major in?” Cell biology. I didn’t know. To me in the 1980s, that there was a major in cell biology in any university was a revelation. “What do you want to do?” She said, “I want to do medical research. I want to do biologic research, biochemistry.” She asked “Why did you go to medical school?” I told her that I didn’t want to chase grants for the rest of my life.

NB: An example is someone in the academic community losing his grant. Do you realize the devastating impact on somebody’s psyche? So I would like to build programs with staff – I don’t know how you can do it. It can be done if you start out, again, to put a lot of money into it, a lot of money, and begin to ask what careers you can offer people. And you have to accept that if you take in a hundred who are the intellectual equivalence that were in the clinical associates and Research Associate Program, maybe 50% will have a successful research career.

BSP: And these..

NB: Research is very demanding.

BSP: So these days the M.D./Ph.D. – the number of M.D./Ph.D.'s are declining?

NB: I don't know. I'd have – there's a program in the GMS institute the M.D./Ph.D. program. I don't know what's happened to it, because I think as indicated to you I'm not convinced that's the route I would recommend.

[low audio]

BSP: We talked about the relationship between NCI.

NB: NCI and NIH?

BSP: The relationship between NCI and other institutes.

NB: Yes.

BSP: Right after the Cancer Act. But in general, while you were at NIH how can you describe the relationship? Is it changing over time? NCI at one time – well, when it was created in 1937 it was separate from NIH.

NB: Oh no, it wasn't separate.

BSP: It was a separate division at NIH –

NB: It was part of NIH.

BSP: When it was created?

NB: I think if you look you will find that is was part of NIH.

BSP: There is a Public Health Service and there is a division and the NIH and NCI – well, it has a separate advisory committee council, and in 1944 it was really – NCI was fully part of NIH.

NB: I won't dispute that history.

BSP: But anyway, I want to know how NCI people perceived themselves as compared to other NIH members, in terms of their independence?

NB: Intramural was one big program.

BSP: I see.

NB: When – at least amongst ourselves. Ed Rall and I envisioned intramural NIH as one large NIH program, and that there will be no barriers from institute to institute.

BSP: So was it easy to move one scientist from one institute to another?

NB: I did it. Particularly with Ed Rall, the first of his people at the Cancer Institute was Mones Berman. Wish I could offer Mones a position but I couldn't. The next was Ira, the next was Bob Goldberger and then Bob Goldberger died. Maxine Singer, and then Claude Klee. From the institute they went to another institute. Dick Hodes went to another institute. Steve Katz became a director of an institute – came to NIH in the Cancer Institute.

BSP: I think for that kind of unity, the sense of unity, the scientific director's relations are very important. You say that scientific...

NB: We were cordial, and no doubt that – we said at our meetings, we spoke our mind. I'll give you an example. I once took in to Bob Berliner a promotion of a technician. "Nat," he said, "Nat, I'm going to sign this, but I'm going to hold my nose."

BSP: So, supportive.

NB: He didn't like it, and I wanted it and I thought I needed it.

NB: You have to remember, when Bob was assigned to the Heart Institute we sat at the same table, down the table, then he sat at the head of the table, you know? You've got to remember. And of course he once said of my division – or even me, it doesn't matter – probably my division – was the last bastion of research in the Cancer Institute. That he told Bob Goldberger.

BSP: How about DeWitt Stetten, he became Deputy Director for Science in '74.

NB: Yeah, just about as I was leaving. Bob Berliner had left.

BSP: Oh really?

NB: Three of the scientific directors know what happened. Don's no longer alive. Ed's slipping, and I may have 80% of my marbles. I'm amazed at what I've dredged up for you today.

BSP: And it seems to me, you know, about Berliner and DeWitt Stetten and Bo Mider, was a sense of community.

NB: Bob Berliner and Gordon Zubrod were both in Shannon's malaria project at Goldwater. They were very good friends. Bob Berliner thought that the cancer

- chemotherapy research was not very good. Did they greet each other cordially? Of course. Would Bob Berliner like the use of contracts? Probably not. Was he probably correct that the cancer chemotherapy research was not going to yield very much very rapidly? Probably correct. Was the virology research good? Bob told me it was. Bob Berliner did.
- BSP: And, in a sense, Bob Berliner and, including yourself, and DeWitt Stetten see the progress of science.
- NB: Yes.
- BSP: Where it goes, and then molecular biology or the study of the biological phenomenon, the microbiology and the use of mathematics and computers, and those others. The kind of vision that they want to bring, was that well shared by other scientific directors?
- NB: I can't answer that. Each one of us brought his own perspective. And I can tell you – I recognize we had to have a mathematical or a theoretical biology, a molecular biology. Doing some type of research that put together the Laboratory of Pathophysiology, and we created the Laboratory of Cell Biology, which Mike Gottesman [?]. I got rid of the laboratory – started taking down or eliminating the Laboratory of Physiology. I wanted to remake biochemistry. I don't know what the other scientific directors were doing at the same time. As I said, we had a new building, we had money, we had some constraints of positions – we had constraints on the positions.
- BSP: And this is going to be my final big question.
- NB: Because I have to be at Building 10 at noon.
- BSP: Right. You left NIH in 1975.
- NB: That's right.
- BSP: But after you left, you still have some sort of contacts with NIH people.
- NB: That's right.
- BSP: And I'm sure that you are very much interested in how NIH is growing and performing, and how especially NCI is doing, and especially the programs you've created. It's kind of your babies, how are they doing? It is a natural emotion. What is your perception, and how, after you left, how NCI, let's start with the small ones, your programs and NCI and NIH in general.
- NB: Okay. My division did very well under Al and continued to do very well. Cancer treatment had not produced the results that people were asking. Whether

they pursued the wrong avenues or pursued them in the wrong way, or else they've tackled a project that's harder than going to Mars. The virologists have become molecular biologists, and in a sense they become a major part of the cancer biology, and if anything is going to have an impact on the future it's going to have to come from the current efforts in cancer biology, which have been extraordinarily successful, while at the same time the treatment – what we can do for patients – hasn't improved very much. NIH still is a major supporter of research throughout the academic community. It has a major research establishment here; at least it has buildings, laboratories and people. It may have a good leader in NIH. There are some who question the leadership of NCI. The NCI director has reduced the intramural budget by 5%, which has an enormous impact, demoralizing. Would I have done it? No. If were here, would I have opposed it? Yes. That's what I can say. The Heart Institute, in terms of what its impact on people has been there's a lot less cardiovascular disease today than when I left, by an enormous amount. Has NIH does anything to make aging any better? No. Can we treat multiple sclerosis or Alzheimer's disease or dementia, other than the Alzheimer's? No. Are we dealing with chronic disease that is very difficult to deal with, very difficult to evaluate the impact of any intervention? Yes. That we've done – we've been very effective in the potential for reducing the impact of cancer, but we haven't gotten rid of tobacco. Tobacco will reduce it by a third, if not more. And we didn't do the tobacco ones – American Cancer Society essentially did it. So that's my public pulpit.

BSP: At some point – well, in the 1960's and '70s intramural scientists were asked the question, "Why do we need an intramural program?" And it was especially challenging in the '80s, and there was a committee to discuss whether it's better to privatize the intramural program. And so there was a discussion going on about the existence, the rationale of the intramural program.

NB: The academic community would love nothing better than to see the intramural program go. If you'll excuse me for just a minute so I can go to the washroom.

NB: Just a minute, I'll come back, because you've gotten me interested.

BSP: So, could you comment on some people who are asking why do we need intramural programs in America while extramural programs are okay and the universities can take care of all the research. How would you respond, while you were at NIH and after you left NIH?

NB: I can't repeat what I said in the hall but I said essentially, "Don't destroy success." This is a model. The other model is Mill Hill, and the Walter and Eliza Hall in Australia, where half the budget comes from the Australian government. Mill Hill, at least when I was there, was entirely from the Queen. Now, each one of them – there were other models in Britain, up at Cambridge, some of the molecular biology labs – stable support from the government. Operative phrase is

stable support. Another operative word or phraseology is an independent review. I had a board of scientific counselors. I got the reviews that I needed, and sometimes got what I didn't want, but I got reviews.

BSP: And you implemented some of the devices?

NB: Yeah, sure. Why do you think I did very little for two years about the biochemistry lab?

BSP: I see.

NB: Or the physiology lab didn't survive.

BSP: It's not just out of your wing, but it's based out being independent?

NB: In a sense, I would take a unit to them and get their comments, and they would get my opinion. They often got my opinion. I tried to get an independent one and then we would share our views.

BSP: Thank you very much for this interview.