

Joseph Edward Rall, M.D., Ph.D.

This is the first interview in a series on the career of Dr. Joseph Edward Rall. It was conducted on 15 February 2000, in his office on the sixth floor of Building 10, National Institutes of Health, Bethesda, Maryland. The Interviewer is Dr. Buhm Soon Park.

Park: First of all, thank you very much for allowing me to have an interview with you. This is for my research project for the history of the Laboratory of Microbiology at the NIH, and I'd like to have your observations as an NIAND director for intramural scientific research and also the DPD director for science at NIH. And I want to have your views on intramural research at NIH in general, and also your view on that particular lab as well as your experience at NIH from 1955.

I'd like to start with your background, educational background and family background, even though you already said that to someone elsewhere. What or who influenced you to become a physician and also a researcher?

Rall: I suppose it was my parents and my relatives. But you must not speak about the Laboratory of Molecular Biology at NIH because there are at least two of them. One is the one which is now in the institute called NIDDK. There's another one in the Cancer Institute run by Ira Pastan, who was in my old laboratory 35 years ago, and which is also an excellent laboratory, just to sort of clarify the definitional problems.

I suppose I had two uncles who were physicians, one cousin who was a lawyer, and he was very interesting, so I thought I'd go into law for a year or two when I was in high school. Then I switched to being an M.D. and was rather sort of not wildly excited about anything one way or the other. One of the things that actually I found most fun in college--I went to this small college--was the professor of physics, who was a very nice guy, and who'd take a sabbatical and go to MIT or Paris every five or six years. He was interested in the structure of water, and it was just an interesting problem and not totally resolved, liquid water. The structure of crystalline water, namely different kinds of ices, was reasonably well resolved. And, of course, the gas phase is no particular problem as far as I know. At any rate, he read that--we're now talking about the mid-late 1930s--water had to be treated in topological terms. So he saw and talked to a math professor, who was an old friend, "What do you know about topology?" and the math professor said, "Actually, not very much." I should say topology was just beginning to emerge in the early '30s. And there was a Polish guy who had written a book.

So another professor of physics and math, the three of them got together, I think corralled a math major and a physics major, and then invited me. I wasn't either a math or a physics major. And so we met once a week from seven to eight, from seven till nine, or something like that, at night, and went through the beginnings of topology. And I found that really

extremely exciting. And there were these full professors, very intelligent, Ph.D.s, and I was a young punk probably about 19 years old studying topology with them. So that was sort of... Of course, I never did anything with it. I never [used] topology in my life. I'm not sure I understand much of it anymore.

Park: So you studied topology.

Rall: This was just at night, no credit, no nothing, couldn't say very much about it now. But it sort of gave me an insight into how serious scientists try and do science, even though this is mathematics and perhaps it's not quite science, how you think and study.

Park: And you go to medical school?

Rall: Then I went to medical school. And then I got involved in the Pharmacology Department there. I need to make a little money because I ended up with a master's degree in pharmacology. And then the professor of medicine somehow got to know me because I'd borrowed his cardiogram to do cardiograms on dogs. And so I worked for him, too. So it took me four years to graduate because, in spite of going to summer school for a couple of summers.

Park: And you also took a Ph.D.

Rall: That was later, when I went to Mayo Clinic.

Park: Yes. And was it usual or unusual to have M.D.-Ph.D. double degrees at the time?

Rall: A little unusual. It was _____.

Park: And so, for your Ph.D. degree, what subject did you study?

Rall: I was interested in iodine compounds, and paper chromatography had just come up then. And so I chromatographed blood and serum and urine, looking for the major iodine materials _____, and it was pretty primitive work. But at that time, paper chromatography, I think, had just been published two years before. Martin and _____, I think, got the Nobel Prize for it.

Park: And when did you get the degree?

Rall: I finished there in '50. But by the time I finished my thesis and got it approved, etc., was '52, if I recall. But I left the Mayo Clinic in '50 and went to Sloan-Kettering Medical School.

Park: So you did your research at Mayo Clinic?

Rall: Yes.

Park: At the University of Minnesota?

Rall: Yes. At that time, the Mayo Clinic didn't have an academic status, and so they could confer degrees only through the University of Minnesota.

Park: I see.

Rall: So that's why I guess the Minnesota alumni news and everything, and the only time that I was at the University of Minnesota Medical School was when I took a few exams. Then, subsequently, Mayo Clinic became Mayo Medical School, so now they give their own degrees.

Park: Right, right, yeah. That was a bit confusing.

Rall: It's confusing.

Park: Yes. And...

Rall: Another confusing thing is Northwestern University doesn't give you, or at least at that time, didn't give you an M.D. until you'd finished your internship.

Park: Oh, really?

Rall: So that meant I actually finished all my academic work in 1944, and I think the degree was not really granted until '45, when I finished my internship.

Park: And you came to NIH in 1950?

Rall: No. In 1950, I went to Sloan-Kettering Institute and also had an appointment in New York Hospital, Cornell Medical School. And so I was there five years.

Park: Five years there. I see. And who made you come here?

Rall: Well, Hans Stetten offered me a job here, and, oh my, there were lots of laboratories. And at Sloan-Kettering, you had to get grants, and so--they weren't too hard to get: the Atomic Energy Commission, the New York Cancer Society, the American Cancer Society. We never even tried the NIH. They didn't have any money in the early '50s.

Park: Right, right. And--

Rall: So Hans had all these labs and some positions to fill, and I could buy some

equipment and it sounded just terrific. Took a small cut in pay.

Park: So, did you meet Hans Stetten through NIH grant proposal or...

Rall: No, no, no, no. It turned out, an old friend of mine was Rosalyn Pitt Rivers who worked at the National Institute for Medical Research in England, and she came here to work in probably '53-'54 with Fritz Lipmann at the Mass. General Hospital. And somehow she got to know Hans Stetten and I got to know her because she was interested in the thyroid, as was I. And so, apparently, the story I have is that Hans Stetten drove her somewhere, from here to New York, and he said, "I'm trying to get somebody to run a clinical endocrinology laboratory," and Ted Hastert [sp.] turned him down. "Well," she said, "try Ed Rall." So he came to see me, and it was very interesting.

I'd looked at a lot of jobs, and in general, the person who was interviewing would tell you everything they'd done, and you'd say, "Yes, sir, yes, sir, isn't that interesting." And Hans Stetten came up to see me in New York, and he said, "Dr. Rall, there's been discussion around the laboratory about"--and then it was DPN rather than NADP--"about the relative ratios of DPN, DPNH in diabetic animals versus non-diabetic, and one of our people thinks _____. He said, "So, what do you think?" _____ except to think that this guy was a smart guy. And so he sold me right away.

Park: And so you came to NIH as the chief of the lab?

Rall: Mm-hmm.

Park: And I'm interested in, what was your first impression of NIH and what was the reputation of NIH as a research institution in the mid-1950s?

Rall: It was just beginning to get a research reputation sort of in academic circles.

A friend of mine, a _____ a postdoc with me, was Yung Shitada [sp.], and I told him about NIH. "Oh," he said, "for heaven's sakes, they publish half the papers in JBC," which was a little exaggeration. But they were really just coming into the same, and certainly it did seem to be an extremely open place where everybody talked to everybody else, and with great resources. On the other hand, Sloan-Kettering wasn't bad, and it was open. I'd learned a great deal from physical and organic chemists there, my friends, but I hadn't really done much in the way of taking serious courses, which the NIH had available, and so I immediately started taking mechanism of organic reactions, which I'd never had--my chemistry was hopelessly out of date--and some spectroscopy, _____ of quantum mechanics, which I'm not sure I really ever really understood too well. And so it seemed to me the NIH in the early days was a place where there were a lot of young people, and a lot of people who were not adequately prepared for biological and biochemical research and wanted desperately to get everything that was--the tools that they'd missed somewhere along the line. So it was heavily infiltrated with physicians, and many of the physicians hadn't had much basic science, but they were smart as hell.

And so there were all these classes you'd go to, and some of them you would have some very smart M.D.s who had never had the course. And occasionally you'd have an old-fashioned organic chemist who hadn't followed the new quantum mechanical analyses. And so I remember one case in which the young instructor was, after _____ all the electrons, turned around and said, "So, you can see why this is acid catalyzed." And one of the old guys came in and said, "Yeah, I've run the reaction. I'll tell you, it goes better in base." So there was this nice sort of mixture of different talents and experiences.

Park: So, when you came here, the night schools were already established.

Rall: Yes, yes. It was curious because at that time, they were run by the Department of Agriculture, because the NIH didn't have authority to run schools, but the Department of Agriculture did. Of course, most of the teachers were NIH people, but the administration was the Department of Agriculture. So that's why the Foundation for Advanced Education in the Sciences was formed around 1959 or '60. They said, "It's ridiculous. It's NIH people who give the courses, it's NIH people who take the courses. Why is it run...?"

Park: At NIH.

Rall: At NIH, so why... So it's been that way ever since.

Park: So the opportunity to learn the recent science was one of the great attractions of NIH.

Rall: That plus space plus a pretty good equipment budget.

Park: So, you already knew that you had, you would be well equipped and well supplied for your research.

Rall: Mm-hmm.

Park: Was there any other career options for you, like university...

Rall: Oh my, yes. I used to have a folder labeled "job offers." Sure, I had job offers at Yale, at Harvard, several different places. But they didn't look as good as this.

Park: Oh, really?

Rall: Yeah.

Park: And you wanted to spend more time in research...

Rall: Yeah, yeah.

Park: ...than teaching and other administrative things?

Rall: Well, there was almost no administration, and I had some clinical links, but I--and in a sense I missed some of the clinical aspects I'd had at Sloan-Kettering Memorial, but that was...

Park: You came to NIAND at the time?

Rall: Yes.

Park: Was there really, at NIAND, was there kind of a division between the clinical research and basic research, the labs devoted to the clinical patient-oriented research and the labs for pure science, like DNA, RNA, and things like that?

Rall: That's certainly true. And there still is, but at that time, there was a much bigger emphasis on organic chemistry. And ordinarily, Dr. Stetten really didn't think highly of M.D.s hiring Ph.D.s to do their science. We got along very well, and so, actually, I hired a fair number of Ph.D.s, and we didn't do a lot of clinical work. We did more basic science. But we had a-
-clinically, we did some clinical. So in spite of this sort of separation between the labs and the clinic, the major grouping were laboratories under which there'd be several sections, on the one hand, and branches which had clinical responsibilities, on the other hand. And mine was a branch, but Hans treated me as a lab, so that I hired Harold _____, physical chemist; I hired Hans Kahnman [sp.], an organic chemist; Jan Wolf [sp.], who was an M.D.-Ph.D., but really a biochemist.

Park: Do you recall how the Laboratory of Molecular Biology was established in 1961?

Rall: Yeah.

Park: Hans Stetten was the main motive force.

Rall: What happened was that--I don't know where they are. Gordon Tompkins was critical in it, and he'd been in a clinical branch. He was an M.D., of course, as well as a Ph.D. And then there were a couple of first-class Ph.D.s. At that time I guess they were called physical chemists and organic chemists. They later became molecular biologists, such as Gary Felsenfeld and David Davies. And so Hans thought it would be a good

idea to get them together. And Gordon and I both were on sabbatical in France in 1961-'62, and so Hans, I think, set it up in '61. He got some space in Building 2. And then when Gordon came back, he made Gordon head of it because they all loved him. And so that was about that. And then Hans left in '62 to become dean at Rutgers, and so that's when I took Hans's _____.

Park: You know the term molecular biology was something new at the time, wasn't it?

Rall: Yeah, it was indeed. Yes. It was hardly established by '62, I guess, because, although, of course, Watson and Crick [sp.] were well before then, '53, if I remember, Jacoby Mono's [sp.] messenger hypothesis was basically a hypothesis, I think, and things were just beginning to get settled out. It was only about '62 that I think Perutz got the structure of hemoglobin.

Park: Right. So the field is just blossoming.

Rall: Just blossomed.

Park: Yeah. You took Dr. Stetten's job in 1962, and was that at an _____ service _____?

Rall: It took time. But it was fun because I saw all the lab, branch, and section chiefs at least once a year, and so I heard about what they were doing, in addition to what they wanted, needed. They all wanted more space, they wanted more positions. So I learned about what was going on in the entire

institute, so this was an incredible learning experience and lots of fun. But I had less time in the laboratory. I always kept one laboratory, mind you, and usually one postdoc, and in the beginning a technician, but later just one, maybe two postdocs throughout all the years.

Park: Yes. I read your list of publications, and you continued to publish throughout your service.

Rall: Yeah. Not very much, but a little.

Park: So your job as the director of intramural research is coordinating and distributing resources to many labs and branches?

Rall: Precisely.

Park: And are you, were you involved in any planning for research, let's say, "Let's do this kind of research," and then you kind of suggest or give an order to the lab chiefs that, "Why don't you study these kind of things?"

Rall: No, that's not... I don't do that. The only difference is that the Congress sometimes will tell you what you ought to do. For example, for a long time, before I was deputy director or before I was _____ a director, they wanted diabetes research because some very important senator had a diabetic wife. And so we went through that for a long time, trying to get somebody to do diabetes research, till finally we got Jesse Roth [sp.], who was really interested in that.

And then at another time, we were mandated to do research in orthopedic surgery, so I saw all sorts of people. I got a very prominent orthopedic

surgeon from Sweden down. He was very, very good. And so he sort of laughed when I told him the salary he'd make and the fact that he couldn't consult and make a lot of money that way. So finally, when the chief resident in orthopedic surgery at Johns Hopkins turned down the position as head of orthopedic surgery _____, I reported back to Congress, "No sale," and they were very considerate. I'd been in touch with the orthopedic surgery lobbying group here, and it was just clear at that time-- which is better now; at that time, there was no way to hire highly paid subspecialty M.D.s to do surgery; they were making too much money elsewhere. But other than those few forays into applied research, I didn't do much.

I know at one time I felt we didn't have adequate electron microscopy and I wanted to get somebody as an electron microscopist mostly so we could chat with other people, maybe collaborate with other people, and so we got one. I'm not sure it was a great success.

Park: So, how... There was a discrepancy between the salaries of professors in academia and the salaries of NIH researchers, especially for M.D.s. How do you...

Rall: Well, for a long time there was also the Korean War, and that meant that M.D.s had to serve two years in the military. And so the question was whether you wanted to serve in the Army and go to Korea or whether you wanted to come to NIH to do research. So for, I guess, 15 years, we had

essentially the pick of the M.D.s from the best schools in the country. And so when the draft, the doctors' draft, was over, we saw a falloff in the quality of the M.D.s who came.

It was at about the same time when there was sort of a general disillusionment with intellectuality, with research. There was more a feeling of do good and be nice and holism and everything that was the opposite of hard science. But that's gradually, I think, mellowed a little bit, and now hard science is _____.

The trouble with M.D.s, of course, is that, on average, an M.D. owes \$80,000 when he gets out of medical school, so he can ill afford to do research.

Park: Right. They have to make money.

Rall: They've got to make money. Yeah.

Park: Someplace, I read a comment made by Ph.D.s saying that, "Well, at NIH, Ph.D.s are second-class citizens as compared with M.D.s." Is that true? Is there truth in that?

Rall: No, it isn't true, but there's a germ of truth and it differs among the institutes. I don't think you will find that in the Diabetes Institute, the old NIAND, because, as far as I was concerned, it was the science you did, and some of the Ph.D.s were doing such superb science, for heaven's sake. But certainly they feel, have felt that way, and part of that is due to salary considerations. The M.D.s would get special bonuses because they were

M.D.s,--not because they did good research, but just because they had M.D. degrees, and I know that rankles a lot of Ph.D.s and there's nothing you could do about it. The problem was supply and demand, and if we wanted to do any clinical work, we had to try and get M.D.s, and we had to do some clinical work.

Park: I see.

Rall: Not just to please Congress, although that was not unimportant, but really, as the National Institutes of Health, this had to do with the health of human beings and the entire gamut from mathematical modeling of dendritic junctions to taking care of terminally ill patients with cancer. We should really be interested in that entire gamut, which is a broad gamut. That means we should cherish--and in our institute, we certainly cherish mathematicians and physicists or chemical physicists. But at the same time, we had to have some physicians who were interested in patients with diabetes and who were in terrible trouble because their blood sugar couldn't be controlled or people with far advanced thyroid cancer or parathyroid glands is all they could find, etc. So I felt NIH had to expand that entire spectrum.

Park: Right, right. It's amazing, actually, that on the one side, the computer science and mathematicians and all kinds of technology-oriented things and, on the other hand, the patient-oriented kind of traditional medical school-like...

Rall: The other thing I think that was an early idea before I came here--and this building exemplifies it--and that is to try and mix them up. That is to say, you'd have a patient wing here, then you'd have the clinical investigator's laboratories around it, and then in the exterior wing, you'd have basic science. So that way, the clinicians could talk with the basic scientists, who were right next door, and it really worked out very well. Herman Kalcker, Bernie Horecker, Leon Hepple, were all in this building, and so clinicians collaborated with them and learned a lot of things that way. And so I think that's been an important aspect of the NIH, is to make sure that a clinician can talk to a biochemist, a biochemist can talk to an organic chemist, an organic chemist can talk to a chemical physicist, who can talk to a mathematician.

Park: How did that kind of collaboration initiate?

Rall: I don't know before my time, but certainly the physical setup of this building encouraged it. And then, when I first came here not long thereafter, when Hans Stetten was running it, wanted the lab, she said, you know, "We should get our laboratories better together." And so he set up an elaborate scheme whereby each laboratory or branch would host two laboratories or branches every couple of months. And so, in the course of a year, essentially everybody visited with everybody else, and so that got people to know other people in the institute. And we've always been concerned, the NIH as a whole, about fostering this kind of interaction.

I know when I came here; there was an endocrine seminar group. It consisted of endocrinologists from the metabolics for IAND, the Heart Institute, the Cancer Institute, and later, when it was organized, the Child Health Institute, and that still continues, _____ endocrine.

Park: Recently I read an article written by a former NIH postdoc, Harvey _____ at NIH, and if you have any problem or question, you can get advice from top-quality researchers anywhere at NIH. And they are willing to help you. And that kind of openness or intellectual openness sort of characterized NIH, and I wonder, how did it start and then maintained?

Rall: It started, of course, when it was a rather broadly based organization having nothing to do with patients, except, of course, Joseph Goldberger and _____. But one thing I think is the structure of NIH. It's in a sense not a zero-sum game. That is to say, if you get something, it doesn't mean the guy next to you won't get it. There are not a limited number of professors, associate professors, etc. So if you get promoted, that is unrelated to whether the guy next door gets promoted. And so this cuts down on rivalries and jealousies a little bit.

And the other thing is that it's rather homogeneous and not totally compartmentalized. For example, each institute has sort of the gamut from clinical _____, and so this means that there will be some cross-fertilization in that institute. But, naturally, the organic chemists, you know, in one institute are going to be interested in the organic chemists in

the other institute. So there's another kind of collaboration, inter-institute but in the same discipline, and the institute collaboration, different disciplines but in the same institute. And so those double collaborations and interactions I think really make it much more satisfactory and an easy _____.

Park: These days, there are something called interests.

Rall: Yeah. Varmus set up interest groups, which was a good idea.

Park: In the past, there was journal clubs or...

Rall: Oh, yeah. Well, there are journal clubs usually for each laboratory or branch. But then there are some inter-institute journal clubs or data clubs or something like that, but not as many as when Varmus set them up, which was a good idea.

Park: You mentioned the other day about the differences between the academic situations and the NIH situations in terms of the competition and rivalry and the organization structure. When you get down to the lab bench level, how was the laboratory culture different from the labs at the universities? You experienced the Mayo Clinic and Sloan-Kettering and the University of Minnesota and then...

Rall: Well, it was... You know, graduate students are very few. Graduate students at NIH are mostly sort of in the back doors, so there are no graduate students; there are no medical students. For example, many laboratories have medical students either taking a year off for some reason.

_____. There were not as many. There are now more. There were not as many college students who take the summer off. And so there were mostly postdocs, and so this made for a slightly different aroma. It wasn't that different from Sloan-Kettering. I never had graduate students, but they did have there. They didn't have a major influence on the sort of psyche of the institution. The spirit of it was largely, of course, the tenured people and the postdocs. So I suspect the NIH was slightly skewed compared with university _____, with less younger people and more postdocs.

Park: And does that have any implication about doing research?

Rall: A little bit in the sense that... And gradually we began to have less technicians. And so that meant that someone with a B.A. and a Ph.D. and a year's experience in a lab found himself making up standard solutions or cleaning glassware and doing all sorts of scut work that you might have had a technician or a student doing somewhere else. It didn't seem to bother them a great deal, because when you were here, you had great opportunities to do anything you wanted to in general, buy equipment that could be expensive, or supplies, and you could talk to anybody. And in most places, you had lots of freedom.

Park: Yes. I met several senior investigators, researchers, at the lab, and it seems to me that they are, could have built _____ bigger research group if they had worked at universities, but they just kept their groups small and,

at the same time, they got their hands dirty. They did their own research for a long time.

Rall: Precisely.

Park: Until the '60s, and even, you know...

Rall: Well, you find Gary Felsenfeld, who must be 70 years old, still pipetting.

Park: Right.

Rall: Doing everything.

I remember some guy was trying to hire, who was sort of a senior postdoc ready, sort of, for tenure, and he said he was interested in the NIH because he'd go to see the big professors all over the place, and they were in a big office. _____. And he went to see the big-shot scientists at NIH, they were in the laboratory. They were pipetting. They didn't have a big office anywhere. They were working away, support. It's a difference.

But, of course, people like David Davies and Gary Felsenfeld, Marty Gellert; they don't have any administrative obligations to amount to much of anything, and not much in the way of committee meetings, no admissions committees. They're pretty free just to do science all day long, and it makes a big difference. And you don't have to spend years writing grant requests.

Park: And no teaching.

Rall: And no teaching. Well, most of them don't mind that, not teaching.

Park: Right.

Rall: David's given a course in entry crystallography for 40 years.

Park: Actually, I'm taking his course of the _____ semester.

Rall: I took quantum mechanics from Gary Felsenfeld.

Park: Oh, really?

Rall: Gordon Tompkins was with me in the course. We both did.

Park: Well, in terms of hierarchy, do you think of Dr. Tompkins more higher than Dr. Felsenfeld at the time?

Rall: He was much higher than we were. He knew it and we didn't.

Park: I see.

Rall: I have _____ always, the hierarchy really depends on who knows most about what you're discussing, and that means that the laboratory doesn't get away with saying something unless he can back it up. And the hero in the journal club or data club is the guy who knows the most about that particular thing.

Park: So intellectual authority is more important.

Rall: That's one thing we've tried to emphasize all along.

Park: I see.

Within NIAND in the 1960s, the Laboratory of Molecular Biology was a young laboratory. And was it any different from other labs in terms of culture and...

Rall: It's hard to say. It's never been great, as far as I know, on having laboratory picnics and laboratory dances or anything like that. But it's

been great just because (a) it was a particularly burgeoning field at the time it was formed. More was happening in that particular area than anywhere else; irrespective of what group you're talking about, just science itself. And there were particularly able people, Gary and David and Marty, and then they got Jun-ichi Tomizawa, who must have been here 15 years, and who was absolutely sensational. And now they, of course, have Kioshi [sp.] and they got Bob Martin. Bruce Ames left, which was unfortunate. He's very smart. And who else left? Gordon was a major loss. Gordon and Bruce were the major losses. But then they got Tony Zoll [sp.] for a while and _____ Zuchi [sp.], and they're getting some young guys who I don't really know. I guess there's an x-ray crystallographer that they're getting. Oh, and Mike Krause. He's absolutely _____.

Park: Could you comment on Gordon Tompkins? I tried to collect something about him, but he died in 19____, and everybody commented on him as a fantastic guy, very good musician and very charming. Could you comment on him?

Rall: Sure. He was one of my best friends. We were in Paris together on sabbatical, different laboratories. That's how we got to know each other.

Park: About the same age?

Rall: Same time, '61, '62. Gordon, you know, got his M.D. first, and I remember the story at Harvard. The night before a big exam, he'd get

tired about eight o'clock and practice his saxophone and drive all of the Harvard students crazy because they knew he was going to get a 98 on the exam the next day. There he was in study all. He was playing a goddamn saxophone, which interfered with their studying. But he was always so kind and generous, enthusiastic. But he was really smart. He almost never forgot anything.

And he was always particularly sympathetic to friends and postdoc science. They'd say, "Oh my, things aren't going well." "Well," he said, "what have you done?" They'd say, "Well, I just did this." "Well," he said, "that could be interesting." So by the time they were through with it, they were all excited and jazzed up and back in the lab for 18 hours. He always saw the bright side on everything. And he intrinsically liked people. He read everything, forgot nothing. That's--Gordon really had a remarkable mind, I think. Also, he had a remarkable optimism and sort of a genuinely childlike way of looking at things, which is obviously the best way, because as we grow up, we probably learn more bad habits than we learn good facts. The idea is to learn less bad habits and more good facts. So, charismatic was the term for Gordon.

Park: Right, right. He was charismatic, but he's not imposing.

Rall: Oh, no, no, no, he never is. He was never imposing or domineering or anything like that, very casual.

Park: I think that influenced a lot in the beginning of the lab.

Rall:

It did indeed.

I remember his wife was a musician and a painter. She lives in California, and I've kept up with her, Millicent, and she was sort of avant-garde, etc.

And one night, so the story goes, she got Gordon to attend one of these sensitivity sessions or something, and so it began late at night. Finally Gordon said, "Okay. When do we all take off our clothes?" And they thought that was _____, so he fell asleep.

Park:

I'd like to talk about 1960s NIH, and that was the years when James Shannon was the director, actually, from 1955 and until 1967, and somebody called that years as the golden years of NIH. And I've read an article written by James Shannon himself, and he himself said that the years between 1955 to 1958 was the crucial years for NIH. Well, I wonder, how can you characterize the legacy of James Shannon in terms of making NIH grow very fast and the research _____. And could you comment on that?

Rall:

Sure. I'm not sure my comments are very authoritative. I usually am, of course. In the first place, he was a very smart, savvy, down-to-earth guy, and he cultivated the Senate and the House people. The senator was Senator Hill, and one of the main House people was Fogarty, John Fogarty, and so he was very good friends with them. And also, he didn't neglect the permanent staffers. For example, when senior staff of Mr. Hill's I think had diabetes and was taken care of here, when he was

admitted to the hospital; Shannon went by to see how he was that afternoon. So he was politically adroit, you know, sort of a politically knowledgeable, savvy Irishman.

He'd also been a good scientist, and he sort of knew good science. He also was without pretense.

I remember seeing him, I suppose, in the early '60s. I said, "Jim, you know, there's nobody doing any work on oxidated phosphorylation in all of NIH." He said, "What the hell is oxidated phosphorylation?" He hadn't the slightest worry about being caught not knowing anything. He had plenty of self-esteem. And, of course, he'd chosen pretty _____ well early on. As a matter of fact, he may be mistaken because some of the critical things were '50 to '55, when Shannon was going around to the medical schools saying, "Who are your brightest guys? I can keep them out of the draft, and they can work with you for another year and then they'll come to NIH." That's how they got Don Frederickson, Bob Gordon, I don't know, half a dozen people who ended up playing very influential roles at the NIH.

Park: And did he have a kind of vision for doing basic research for the advancement of medical science or...

Rall: I don't know. I'm sure it was probably due to him that the Clinical Center was set up the way it was, to encourage interaction between basic and applied and clinical _____, so I'm sure that was part of his agenda. He

never particularly articulated it, but I think he made it happen--or at least I didn't hear him articulate it. He was relatively inarticulate. He'd sometimes give an impromptu talk at the institute directors' meeting, and after 10 minutes you weren't sure what the hell he said.

Park: But he was influential.

Rall: He was very influential, and in absolutely the right way.

Park: The late 1960s and early 1970s were not good years for NIH. In some way, the Congress pressed NIH about the social accountability of research and what is the relation between your research and the disease and how all kinds of pressures...

Rall: That's still going on. I'm not sure it's worse then than it is now.

Park: Right.

Rall: It might not be as bad. We didn't have quite as many interest groups, patient advocacy groups. At that time we had the diabetes, the juvenile diabetes, very powerful. But now there are so many of them, and so your Congress is inundated with the special _____ and can't help but respond. That's Congress. Part of their *raison d'être* is to respond to the public will. And so I'm not so sure that what right now isn't worse than it was then. We've got huge complaints that we don't do enough on the chronic fatigue syndrome. Women are worried that there isn't work done on women. Now, of course, it turns out breast cancer has always had 20 times more support than prostate cancer, but women don't care about that. They just

feel they've been excluded from clinical trials, and that's a big _____.

You have to try and explain that to them. So I'm not so sure that what special interest groups aren't worse.

The only thing that's saved the NIH for the last five years is the exceptionally good budgets, so that under those circumstances, it's easier to please everybody. If you've got a stationary budget, then it's much harder to please people.

Park: Right, right. I have read your summary of the research activities at NIAND in the annual report of the progress, activities, annual report of progress, and...

Rall: You know more than I do because I've forgotten all this.

Park: I don't know whether you remember writing this.

Rall: Yeah, I do.

Park: Yeah. And you were concerned about the intellectual dislocation. I think that phrase captured the situation at the time very well. And could you say more about that?

Rall: No. _____ hormone action _____. Yeah, that was a bad year. I don't remember, of course, _____. And it's certainly true that there were years when all you did was molecular biology, where we actually did lose positions. And I don't know how much you want to go into that, but that's been an interesting thing. In '73, we really had two kinds of positions, three kinds of positions. One were regular service, civil service positions.

Other were commissioned officer positions, which were used for people who might get drafted. And the third were visiting fellows, which didn't count as a position, but they had to be foreign and within three years of their degrees.

And then, gradually, partly when I was in Building 1, a lot afterwards, it's been opened up so that you now have all sorts of positions which are not positions. So some years ago, the OMB, the Office of Management and Budget, gave up on trying to control NIH from the position standpoint because back in '73, there were so many positions, and that was very constricting, because otherwise you'd only hire visiting fellows, and that didn't take care of American postdocs, it didn't take care of technicians, secretaries, senior people. You know, 90 percent of our employees were counted. And so, then, because of intramural research trainees mainly, American citizens couldn't get these visiting fellow like non-positions and all sorts of other things, so OMB finally gave up on trying to control the NIH through positions.

Then they tried to control the NIH through the budget, and so they discovered after some years, they could get the President to give his budget to Congress, which gave the NIH, say, the same budget as last year or perhaps a 1 percent increase. And the Senate and the House would _____ that budget for the NIH dead on arrival. And then they'd construct a budget most years--there were a few years when Congress didn't save us,

but most years they'd say, "Okay, we're ready to budget 5 percent, 6 percent. And, of course, the OMB was out of the loop. So, gradually, they realized they couldn't control the budget, tried to control it through the positions. Then they couldn't control the positions or the budget, and so then they came back and tried again, for the President's budget to be close enough to what the Congress might buy so that the Congress wouldn't get angry. But then in the last few years, the Congress has been particularly generous with the NIH.

I think--I don't really know, and I, of course, don't follow these very well anymore. But I have a feeling that it's either an outgrowth or springing _____ from the general realization that a country does well if it does research, and if it doesn't do research, it's going to be trying to rent patents from someone else, the industry will not be modernized, they'll import, they won't export. So research has generally been regarded as a very important good thing for a country to, and so that's, of course, spilled over from industrial medical research. And, of course, medical research actually does pay off, not only in lives saved, etc., but we can get the best biomedical M.D.s or Ph.D.s in the world. They love to come to the United States. And all the industries which support biomedical research, whether it's Packard or Beckland [sp.] or whatnot, are selling things all over the world, so it improves our balance of payments. So I think Congress sort of had understood, you know, not precisely, not clearly, but in a general way,

it's good to do research and it's good to do medical research twofold, because it helps people who are sick and it helps our balance of payments.

Park: How did NIH have industrial competence to do medical research? Did just the kind of knowledge produced here help them to make drugs or things like that?

Rall: It's rather complicated in its sort of--there are a lot of specifics involved. For example, we had in NIAND a group of organic chemists who'd been working on opium derivatives, analgesics, for 67 years. And I guess about 30 years ago, they had something new that looked very good. They patented it so that it would remain in the public. And, of course, no one bothered to develop the patent because the patent was in the public domain.

Park: Right.

Rall: And so if Abbott did all the clinical testing, pre-clinical testing and everything, and got it, Roche could drop in, make the same thing, sell it for a penny less, advertise it more, and so there was no incentive for anyone to develop it. That drug was never developed, never put on the market. It was a lesson to me that, you know, whether we liked it or not, you have to cooperate with industry.

Meanwhile, [NCI] cancer had been cooperating with industry sort of hand-in-glove or glove-in-pocket or whatever because they wanted all sorts of the drugs to test for _____ cancer. But they'd had close relations with

industry for many years, dating back to the '50s. Then, when I was deputy director for intramural research, there was a big pressure for, at that time, all these startup biotech companies that were being formed, and people were getting very unhappy here, particularly the molecular biologists, because they could make thousands and thousands of dollars a year consulting. If they had stock options, they could make millions. And so Jim Wyngaarden, and I decided to see if we couldn't permit consulting under controlled conditions. And, sure enough, we did, and nobody slapped our hand. But we, of course, didn't permit anyone to have equity positions. You couldn't consult for some biotech firm for a thousand shares.

And so, gradually, there'd been greater and greater collaboration between industry and NIH. And then somewhere along there, they set up CRADES, Collaborative Research and Development Agreements, and so sometimes the company would invest a lot of money in giving you technicians and postdocs, and then they'd have first dibs on commercializing anything that came out of it.

I think that's been a good thing, but I'm not sure. I remember Marty Gellert, when this first came up, said, "Well, this makes NIH just like everywhere else, and we're going to lose basic research." I'm not sure, and it would be interesting to see whether Marty thinks that's happened or not. I haven't talked to him about it.

Park: I found the scientists at the Laboratory of Molecular Biology more or less not interested in the commercialization of their knowledge or patenting their research products, and they just love doing their research their whole life.

Rall: It's sort of an old-fashioned attitude.

Park: Right.

Rall: Sol Berson, along with Roz Yallo, who was a long-time collaborator, developed completely a radio amino acid. They never patented it. Had they patented it, they would have made at least \$10 million. And the guys in molecular biology are sort of like this. They want to do the science and they've got enough money to live comfortably. Screw everything else.

Park: Could you say something about the Molecular Biology Laboratory in the Cancer Institute?

Rall: Oh, sure. Ira was a young clinical associate with me, and then he went with Child Health, gave him a big lab. Then he went with the Cancer Institute, where they gave him a bigger lab, and just a very bright guy.

He's perhaps a little more applied than some of the others.

He started out, of course, with Harold Varmus as his postdoc on astringent response in cyclic [sp.] ANP effects in bacteria and cyclic ANP binding protein and all that, so they were really very, very nice work, lots of quite fundamental work. And then he's gotten very good people, including Mike Yarmolinsky, whose very fundamental interest in phage, including

shaykar [sp.] _____ but very basic phage. And then Susan Gottesman was in his lab, Mike Gottesman, and lots of work on immunotherapy for cancer. So it's a dynamic lab.

Park: When did he start? Do you remember?

Rall: He started in the Child Health Institute probably about '67 or '68.

Park: I see.

Rall: And then his laboratory in the Cancer Institute. I was at, I think, the 20th anniversary of the founding of it last year, in '99, so it must have been founded in '79 in the Cancer Institute.

The other thing about the Lab of Molecular Biology back some years ago, actually not long after Gordon left, I set it up so that it had a rotating lab chief because they were all strong people, and so they'd rotate. And, of course, everybody, all the decisions were collegial anyway.

I think now they've decided that it's easier for--I think Gary is now the permanent lab chief. It's probably was easier to go back to the original. But for, I suspect, 20 years, it was very successful as a rotating lab chief, and there aren't many labs going to do that because someone will be too strong or not strong enough or etc.

Park: So the idea of rotating chiefs was first implemented there.

Could you compare the 1980s with the 1970s, the 1980s when you were the deputy director and the 1970s when you were intramural research director?

Rall: I don't know. I suspect maybe my memory is not precise enough in terms of the time spans involved. But _____ gave me to read or what I've written, I do recall that in the '70s there were some times when we'd have restrictions, mostly on physicians but sometimes on budgets, and the '80s were more expansive times. But that made less difference _____ because I always felt that a time of retrenchment was a time where you sort of cut down the poorer performers and you didn't touch the good ones. Molecular biology never lost any space or positions during those. But some other laboratories or sections or people in the laboratories had a hard time. They'd lose everything because it's a good time to tear down the deadwood. And [if] you do that, you can support adequately the first-class people.

Park: Right, right.

Rall: And so I think those are times which sound worse than they really are if you're not too egalitarian about it, if you're meritocratic rather than egalitarian.

Park: I see. When you took the position of deputy director for science at NIH, was it a kind of position to coordinate among the institutions, not just the labs and chiefs and small scale, but the NIH scale?

Rall: Yeah, yeah, that's precisely true. One of the things you try to do is try to keep everybody sort of going the same way because it really isn't possible for one institute to do something that's wildly different than any other

institute, and you don't want to get jealousies, etc. And, of course, the Cancer Institute is always one that's liable to get out of control because they have this enormous public and congressional support. But they've had some very good leaders. But that was one of the _____ the promotion process regularized so that some institutes could promote somebody who had no credentials.

Park: Did you keep your lab while you were doing...

Rall: I always had one module and one or two postdocs.

Park: I see. And spend some time there.

Rall: Yeah, yeah. I never had a big lab. I never had more than two postdocs in my life.

Park: I see. I read reviews made by outside committee say, National Research Council Committee on Intramural Research at NIH, something like that, and I read that, those kinds of documents, in 1965 and '76 and '88. I don't know whether that my collection is complete or not, but I had, at least I got a sense of how NIH intramural research was viewed by outside peers, especially the university researchers. And their view generally is that the intramural research program is excellent. There are so many good people. But we should not make it too big. We should kind of restrict it in some way and we should have them by managerial improvement and things like that. I read--there is some, throughout the time, there is something in common in terms of commenting on the excellence of intramural research,

and at the same time, well, NIH should, focus on extramural things. I don't know.

For me, the main distinction between NIH and NSF, the National Science Foundation, is the intramural research program. And without it, it's just a _____.

Rall: The grant system is different here.

Park: Right.

Rall: Well, we had intramural scientific counselors, and I remember I was particularly interested in getting first-class people, and I think I had more women than anyone else, but they were first class: [unintelligible], Ruth Sager, Joan Steitz, Lucy Shapiro,--very good people. At any rate, I thought they ought to be first class, and I remember one time someone said, "Ed," he said, "do you know that everybody on your Board of Scientific Counselors is in the National Academy of Science?" Bruce Alberts, the president, who's one of our scientific counselors. Jim Watson is a scientific counselor. And when I got to be deputy director of intramural research, I discovered some of the Cancer Institute science board of scientific counselors were totally undistinguished. And so the question is, you know, what's the makeup? Before you read what they say, see who they are. Even if there are some hacks who are friends of the guy who appointed him, what they say may be irrelevant. But if they're really independent scientists of considerable stature, you have to pay more

attention to what they say.

Now, of course, just in the last three or four years, the boards of scientific counselors have acquired so much power that intramural scientists are complaining. They don't spend as much time preparing for a review as they did if they'd have to write up a grant. They end up having-- a laboratory has a packet this thick, and that's what we're [doing].

Park: I see. When did the Board of Scientific Counselors review start? Was it started in [?]

Rall: It must have started in '60 or '59, because I remember there were boards of scientific counselors before I was scientific director. Hans Stetten had nominated a group, and then I carried on with that.

Park: And I read some of the reviews, and there was _____ suggestions _____ the changes. And I don't know how much those suggestions affect the policy changes at NIH.

Rall: I don't know. I think not a great deal in the '70s and '80s, but in the '90s they've been very important. They've been dominant in deciding whether people get tenure or not. They're probably a little less dominant in deciding which laboratory gets more space or less space or more people or not, but certainly in tenure decisions, they have a major role.

Park: I see. There were from time to time attempts to create a graduate school at NIH, and Hans Stetten made a record in 1976 about the intramural research program, and it is kind of geared toward proposing a graduate

school at the NIH because intramural graduate research program is essentially about teaching at the price of _____. This is _____ NIH.

Rall: Hmm. I don't think I've ever seen it.

Park: Yeah. I got it from his file. Originally there were some interruptions.

Rall: August '76. _____. Well, this is very interesting. No, I haven't seen it.

Park: And the final. It's very interesting that the ways in which Hans Stetten justified the existence of the _____ for intramural research. And he says that, he compares it to _____.

Rall: He compares it with what?

Park: To the Everest.

Rall: Mt. Everest?

Park: Yeah, Mt. Everest, and that we climbed up the mountain because it's there. We do intramural research because it is there. It is because it is there. And because it is there--the final chapter is, the title is "The Intramural NIH as an Educational Institution," and he proposed to create, to make NIH as a degree-granting institution. And I wonder how that idea was received by NIH peers and also by outsiders.

Rall: It was mixed, but I think most NIH people were in favor of it. But I don't think Hans did anything about it. I, too, when I was in his position, thought it was a good idea. And there'd been, you know, an attempt in, I think, the early '50s to do this, and the deans of the medical schools or _____ schools dissented and said no. So the Rockefeller University--you

know Rockefeller Institute had become the university, so I went to see them, spent a day or two there. This must have been in the late '80s. And they said, "Gee, what a good idea," and Tony Cerami said, "Well, you know, I'm dean and it doesn't take more than 15 percent of my time. As far as I can tell, we only have two full-time people in there. Go ahead." So I called some of my friends at Harvard, and they didn't seem too opposed. And so I was about to try and do something about it when Bernadine kicked me out so that I couldn't do anything about that, because Phil Chen knew somebody who was a brother dingo and we thought we had a way to get legislation introduced. But I tried to prepare the way. Then, when I heard what Varmus did, it was a thorough disaster _____.

Park: Yeah. It was _____ Varmus was trying to...

Rall: Yeah, and lost completely. And, of course, he didn't after. If he'd done his homework beforehand, talked to Shirley Tilghman, and the first explanation Mike Gottesman gave was, "We will get minorities." Gary said, "You have minorities? We're trying like hell to get minorities." I don't _____ that. Why should you be more successful?" But he should have said, "We're not trying to get minorities any more than anybody else. But this is going to be sort of a different one. We expect you to be more like the Rockefeller at Cold Spring Harbor than anything else because people are going to be totally independent; they're going to be treated virtually like postdocs. We'll have courses, if they need them, FAES,

theres all these courses. But it's not going to be a rigid Ph.D. program.

It's going to be a program for people who are independent enough to carve their own Ph.D., and we're not going to be in any competition with you.

It's going to be small." I think he could have sold it.

Park: Why that idea was coming from time to time?

Rall: Well, everybody comes here from universities, so they're used to graduate students because they were a graduate student. _____ they had their own graduates. Everybody comes from there, so you can't help but think it's a pretty good idea. Not everybody's in favor of it. And I'm not sure, actually. A small graduate school--I would anticipate a graduate school of no more than 50 or 75 students, maybe 100, that's not going to make a huge difference one way or the other. But I think for some people, it might be nice.

Park: Just curiosity. In the 1960s, the annual report of NIAND and NIDDK started in 1951, and it went on until 1961. And there was a gap in 1961 and 1967, and there was no annual report published or would have listed in the NIH library or NIH Historical Office. And I couldn't locate anything about the annual report at that time. And I think it is common to other institutions like Cancer Institute or AID.

Rall: They had all of them.

Park: No, no. There was also the gap.

Rall: Oh, really?

Park: Yeah. And I wonder why. It was a part of policy?

Rall: For the life of me, I can't... There was some worry that nobody paid any attention to the annual reports, and you'd spend a lot of time writing them up and nobody read it. I think Hans Stetten said he was disappointed to see it or interested to see them being used as a door jamb. They were thick and heavy. And so I don't know what happened. And, obviously, mea culpa, but I just don't have any memory of it.

I've been trying to think. I did write out some justification for the intramural program in the '80s, and I don't know whether--I don't think it was ever published.

Have you seen this?

Park: No. Can I have a copy?

Rall: Yes, you may. _____.

Park: Oh, excellent. I'm almost running out of my questions prepared. Probably I may have more questions in the course of my research.

Rall: Yeah. I've got a few things to do.

Park: Yes.

Rall: Look. Why don't you read that over and go over what's on the tape recorder, and if you want to come back, I'll be here.

Park: Okay. Well, thank you very much for your...

Rall: A pleasure. You have really got a lot of the highlights, I think, of important intramural research.

Park: Right. Thank you.

Rall: Okay.