NIDDK

Oral History Project

Interview with Dr. Phillip Gorden

Conducted on September 24, 2019 by Kenneth Durr

KD: This is an interview with Dr. Phillip Gorden for the NIDDK Oral History Project. Today is September 24, 2019 and I'm Kenneth Durr. Dr. Gorden, thank you very much for taking time to talk today.

PG: My pleasure.

KD: I understand from your resume and from speaking with you that you're from the rural South and I want to start with some of that background and talk about how you grew up and how that led you to a career in science.

PG: My father was an immigrant from Ukraine back in 1922. He was only 12 years old when he came over and he worked with a brother in a tiny town in Mississippi until he was old enough to go into a small business of his own in a town named Baldwyn, Mississippi, that's spelled B-A-L-D-W-Y-N and not like the piano. This was a wonderful, very small community of about 2000 people and we were the only Jewish family. So that was a little bit of an unusual kind of mix for this community to welcome in a Jewish family, and it was a wonderful group of people. Of course, the community was completely segregated at that time. This was in 1933.

My father was just a fantastic person. He worked all the time in trying to get his little business started. It was the height of the Depression in the South and no one really had any money. Everything essentially was bartered. There was this whole series of barns in the back of his store where we had livestock for bartering. My mother wasn't able to participate very much in my upbringing, but I had the incredibly good fortune of having two people, an African-American lady and an African-American gentleman, who were in

some ways my auxiliary parents. They had no opportunity for education and neither did my father. But they possessed a kind of wisdom and kindness that was really something a child needed at that time. So that really allowed me to manage in this community where there were very few resources, certainly from an intellectual point of view. But it gave you a grounding of human nature, and a realization of the trials and tribulations of life. I experienced firsthand the kind of difficulties my African-American auxiliary parents had.

Fortunately, this northeast part of Mississippi was not the part of Mississippi that had such a terrible history. It didn't have the violence that went on in so many other parts of the state. So that was good. Actually, I was born in the town adjacent, just a few miles away, Tupelo, Mississippi, which has the fame of two weeks later giving birth to Elvis Presley. So Elvis Presley and I were born within two weeks in the same hospital in Tupelo, Mississippi, and there are a lot of Elvis stories. We don't have time to go into all of them now, but there are many of them.

KD: So you may have rubbed shoulders at some point?

PH: We didn't rub shoulders but it almost seemed like we did because there are so many stories, and in fact even in the last several years there's a hardware store in Tupelo that if you walk in the first thing they ask you is if you want to hear the Elvis story, and of course you do, and they'll tell you the Elvis story of how he got his first guitar in Tupelo. My children loved this story and insisted we visit the Tupelo hardware and listen to this story. So I felt like I actually kind of knew Elvis, even though I never formally met him.

KD: He used his guitar to get out of Mississippi.

PH: Absolutely.

KD: You used something else. When did you start to think that college may be an opportunity for you in pre-med?

PH: I grew up next door to a general practitioner and I became very close to him. He introduced me to medicine. There weren't that many different opportunities. I participated in everything in high school. There were only 29 people in my graduating class. I was on the football team and the basketball team. I really wasn't very good, but you didn't have to be very good, all you had to do was show up. I did that and I spent a lot of evenings in the pool hall. There weren't a lot of opportunities to go to libraries. There were no libraries.

I had never been to Nashville before, but I knew one person who had gone to Vanderbilt, so it seemed reasonable. No one in my school had ever been out of state to college, so I thought, why don't we give this a try. I listened to the Grand Ole Opry on Saturday nights. Maybe Nashville will be a good place to go. When I was accepted to Vanderbilt my parents took me to Nashville for the first time and introduced me to the college dorm and there I was. So now I find myself moved from this small town to a totally different kind of environment that was rather difficult because I had never experienced the intellectual challenges that I was going to face. It was a difficult period for me.

But fortunately, during that period I met a young woman, a beautiful young woman who was then going to become my wife Vivian. We're actually celebrating our 60th wedding anniversary this year. We were married in Nashville and she's the love of my life, and it's been a “we” history. It's not really a “me” history, it’s something that we’ve done together since that time. We were there in Nashville. She taught school and I finished medical school. Vivian and I graduated from Vanderbilt University and our two sons graduated from Vanderbilt Medical School as I did. My father said, "I've never been to school and I've been to five Vanderbilt graduations." I said, "The fact is that you made all this possible," which was really the truth.

KD: Undergraduate was difficult.

PG: Undergraduate was extremely difficult at first because I had to rapidly adjust to a new environment. Everything had been so easy for me in a small school because there was

really intellectually no challenge at all. Now all of a sudden I was up against this wall, this challenge of education. I knew I wanted to go to medical school, but it looked like it was going to be hopeless. But the reality is that I was the last person accepted into my medical school class. There were only 50 students in my class at Vanderbilt. Basically, what happened then is that medical school became much easier for me. I actually graduated in the upper 10 percent of my class.

KD: Had you started thinking about scientific research at that point while you were still in Vanderbilt?

PG: I was exposed to some really incredible people, Grant Liddle for instance, who was probably one of the foremost figures in endocrinology even today. He had come from NIH just a couple of years before I was a junior medical student. David Rogers had come from Cornell. He was Chairman of the Department of Medicine. So there were some really seminal people on the faculty at Vanderbilt. Vanderbilt was and is one of the outstanding medical schools in the country without any question.

Vanderbilt Medical School was a wonderful experience and I was just totally immersed. I loved it. I worked very hard, but I just loved it. I had on my white coat and started to see patients, and that was very exciting to come out of this basic science into clinical medicine. When I was a student at Vanderbilt the wards were still segregated. Actually, about the time we left Nashville the schools were beginning for the first time to integrate. So now you could see this community which was pulling together in a very important way and was really in the forefront of a more sane form of desegregation. This history in the South is such a terrible history of segregation. Now you're beginning to see big changes and society began to open up. Obviously, it didn't happen all of a sudden, but it did happen.

KD: Had you done any research at Vanderbilt?

PG: I had worked to some extent doing more library type research with Dr. Burton Sprofkin, a neurologist, who I had gotten to be very close to as a medical student. I hadn't really participated in any kind of either basic or clinical research. Since people like Liddle and Rogers were very important clinical investigators, those things rubbed off. You realized that there were people who were real mentors and you began to understand to some extent what mentorship is. So not only were you learning the basics, but you were learning something about the process in which we all hand off to the next group from people who were really that good.

KD: Speaking of handing things off, you're off to Yale as a Resident and you're in a whole new group. You must have had this experience happen all over again in a bigger way. Tell me about that.

PG: Yale was an incredible new experience for Vivian and me. We had never been out of the South. We were exposed to a much more cosmopolitan atmosphere. We were close to New York. We could go in and enjoy the theater. We could do things we had never done before, and fortunately it was a very defining experience for both of us. I worked very hard. We worked every other night, but every minute we had off we were always doing something exciting.

Again, we were exposed to an extraordinary group of people, both those who were my peers, but also faculty. It was Paul Beeson, one of the legendary chairmen of medicine, who decided to leave Yale and go to England. He loved the practice of medicine but as Chairman of Medicine his main job was to raise money. He became the Nuffield Professor of Medicine at Oxford. In fact, I was supposed to go with him. My first mentor as a Fellow was Tom Ferris who went with Beeson to help set up a program. It turns out that my draft board decided I wasn't going to leave the country, so I didn't have that opportunity at the time.

KD: Where was the program going to be?

PG: Beeson went as the Nuffield Professor at Oxford. Tom Ferris went with him and when he came back, he became the Chairman of the Department of Medicine at the University of Minnesota. Phil Bondy, Frank Epstein, who later became Chairman of Medicine at Beth Israel in Boston, and I were working with a whole host of other people of this caliber. The environment that we found ourselves in was just totally different than our experience in the South and we loved it. Both of us worked very hard. Vivian was teaching school again and our oldest son was born in New Haven. We lived in the upstairs apartment of a doctor's office at that time and had other close friends who were in a similar situation.

KD: Did you begin to develop a research interest?

PG: Yes. Research was all around me at Yale. I did three years of residency and then I began a fellowship, an NIH-sponsored fellowship in what was called metabolism, which was a legacy of John Peters who was a legendary person.

Tom Ferris was just a new investigator and I said, "I'd like to work with you." And that got me started. In fact, as a Fellow I was able to present a paper at the most important medical meeting that was always held in Atlantic City, out of the work that we did over the first couple of years. So somehow the fire was being kindled there for research. It was in the very early days, but Tom Ferris and I had already published several papers. Actually, we had published several papers just based on my residency experience and some novel patients we were seeing at time. The experience of doing research or exposed to research, or how people talk about research, was being kindled during that period of time. We spent five terrific years at Yale. Then the next chapter, it was time to do something different.

KD: There was the Draft Board to deal with.

PG: There was the Draft Board to deal with.

KD: How did you work that out?

PG: I did it a little bit differently than what so many people were doing at the time. I managed to get a commission in the U.S. Public Health Service and that then permitted me to go to a Public Health Service facility. Jesse Roth who had been at the NIH for the past three years had a research group and he was just getting started himself. He had worked with legendary Yalow and Berson. Yalow had won the Nobel Prize later for the development of radio amino assay. So he was starting a group and he was collaborating with Ira Pastan who's still here at the NIH, a very distinguished scientist, and they were working on a concept.

Jesse needed someone with clinical experience, and I seemed to fit that bill. I certainly had more clinical experience than anybody who was here at that time. This was in 1966. So I came down and I said "this is terrific. We can work all this out." It was a little bit of a logistical issue, but it all worked itself out. And I came, and I was somewhat of a mentor to a rather unusual group of people, a mentor in the sense that I was the person who actually knew more clinical medicine than they did, even though they were much brighter and more established individuals or certainly would be. The challenge at that time was to establish a clinical service.

So Jesse and Ira Pastan were working on a concept of how hormones worked, so-called polypeptide hormones. And they hypothesized that hormones worked by binding the surface of cells, and this was a totally novel concept at the time. They were joined, in 1968, by Bob Lefkowitz who was a Fellow with the two of them, so the three of them really developed this concept of cell surface binding of a hormone. This was a whole new idea how insulin or all the pituitary hormones worked. Just upstairs was Martin Rodbell who later would win the Nobel Prize for the discovery of the so-called G-protein. So there's this incredible ferment of things that were going on just at the same time. Also in 1968, we had these journal clubs in these tiny little rooms with these incredibly heated projector, these big lantern slide projectors. Everybody was smoking at that time, so you'd have all this smoke and lantern slides, and whatever. And in that group of 1968

Fellows was Harold Varmus, Mike Brown, and Bob Lefkowitz, all who would win the Nobel Prize some years later. This was an incredible group of people to work with.

My role was to try to bring together the relevance of the science that was going on in the laboratory to the clinic, to what was really going on in people and I started to see patients with unusual forms of insulin resistance. And it turns out these patients were the human models of how this process of hormone binding actually was taking place. By using the models of the patients that I had actually been able to bring into the system, we could then subsequently verify that this was relevant to the human condition rather than just a laboratory test tube. So it was a very important period in which we brought these things together to show how hormones work.

We had this concept of proinsulin, a concept that had developed out of a paper that was published by Donald Steiner, who was one of our very important grantees and also on our National Advisory Council later on, who had suggested that insulin was made by way of a precursor. This was heretofore unknown. So we tried to reproduce this so we could show this in humans. Actually, I had a patient who worked in the NIH laundry who turned out to be the model system for this major paper that we published known as this "high molecular weight insulin." As it turned out we verified for the first time that this was true in humans. The same thing had gone on with the hormone receptors. We were able to join the laboratory with the clinic by now having established a clinical program that could match, to some extent, but not quite the same strength as the basic program, but it began to work in that direction.

So there we were and now we were all established. It allowed a ferment of people that you were going to work with later on. It created a network of people, this incredible group of people who were here at the time. All the medical schools wanted to send their most outstanding people to NIH because of the experience they were going to have. At that time we had tremendous support from Ed Rall who was the Scientific Director and Jack Robbins who was the Chief of the Endocrinology Branch.

KD: What was the name of the branch you were in?

PG: At that time it was named the Clinical Endocrinology Branch. I was in the Public Health Service, so I could just continue in the Public Health Service, even though I had finished my military obligation. This allowed me to move into the next chapter where Ed Rall then asked me to become Clinical Director of the Institute.

Again, we were a very broad Institute. We had the Arthritis Branch, which is now the Arthritis Institute at NIAMS, as part of our Institute at that time, a slightly different name than we have now. So we had exposure to many different diseases and many different types of patients, which for me was a total comfort. I was always very comfortable in seeing patients in the clinic, very comfortable interacting with the Fellows, and we developed, I think, a real rapport at that time in terms of developing the clinical program.

The Clinical Center itself was maturing over that period of time. When I first came the Clinical Center really didn't offer all of the support services that you would like to have in a major hospital. And all that began to grow and mature, and I always felt a very important part of that because I was comfortable in seeing patients in other Institutes, and consulting with patients, and being involved in the evolution of what turned out to be the Clinical Center, as we see it today.

KD: One would think that would be difficult because here you had this intensive work in endocrinology, and you were doing insulin. Conceivably when you become Clinical Director it could become almost anything. Isn't that a high bar to get over with each new disease and each new challenge?

PG: I think the phenomenon that was going on, clinical research is hard. It's difficult. Laboratory research with the technology that was available would allow you to make progress much more quickly, so that was a real incentive. You could make progress quicker even with the technology that was available. Clinical research took longer, so you were trying to either develop a career or get from here to there. It’s going to take much longer.

Remember, a lot of people were on two-year cycles and they needed to get something substantial done over a shorter period of time. I think that was part of the reason that this evolved in the way that it did. Clinical research, I think became much more important or available. The technology to do it became more available a little bit later on.

KD: Who were you working with as you expanded clinical research at NIDDK and elsewhere?

PG: We had collaborations with the NCI surgical service, and we were studying islet cell tumors; Sam Wells, Murray Brennan, and Jeff Norton, people that became legends in the surgical field. We in fact had a whole host of surgeons that came through the surgical branch. It then expanded to other programs within NIDDK. There is an important program going on in thyroid research and other kinds of endocrine tumors.

One of the key people in bringing much of this together was John Doppman, who was the Head of Radiology. We needed to bond to bring the endocrine people and the surgical people together. Remember in our Institute we had liver disease, we had kidney disease. We had all these things which, for me were, perfectly normal or natural. But remember that diabetes is the leading cause of kidney disease, nutritional issues of obesity and so forth, all these things are very much interrelated. So for me it was never really an issue of one area versus another. I thought they were all very important and I learned this in the intramural program already. It was part of the base that was created for me.

KD: And you were supporting other people's research in some respects by doing the clinical side of the work?

PG: We certainly had multiple collaborations. Of course, the Fellows that were involved in this, in those initial days when we first started, Ron Kahn was a Fellow, Jeffrey Flier was a Fellow and they were working with us and many others in other areas of liver disease and so forth. We all were collaborative working with each other and supporting each other. In each of the fields we were collaborating with the Neurology Institute with other

people at NIH. The Clinical Center did offer a real opportunity for this collaborative interaction to go on and that was really important at the time.

KD: Something you were involved with was working with acromegaly studies.

PG: Yes. This was another endocrine disease. We were the first to show the efficacy of radiation therapy in the treatment of this disease and studied various aspects of growth hormone secretion, various aspects of the form of growth hormone. So that got us into this whole other area that had to do with insulin-like growth factors that grew up in the laboratory and then we were able to use this in the clinic to study a whole host of hypoglycemic disorders.

This opened up a new field for investigation just like we had done earlier in the insulin receptor area where we had patients who had developed antibodies to the insulin receptor and genetic abnormalities of the receptors. Sometimes it took a while before the technology was available to unravel all this, but you were seeing this from the very ground floor in the beginning. So over time these things began to become more clear, in terms of how they actually operated.

KD: The acromegaly work, how did that present itself to you? Did you say let's look into this and try radiology?

PG: What we did, we collaborated with a group of radiation therapists. We collaborated with radiology because that was important in terms of looking and determining the size of these tumors, and we collaborated with several other individuals in laboratory medicine and so forth. And we had some basic scientists working in the laboratory on these growth factors. It was a way to bring both the laboratory and the clinic together again and it was just another disease. I had this endless interest in a variety of diseases. We were the first to develop a radioimmunoassay for vasopressin, the hormone that conserves water. So we studied a whole group of patients with vasopressin abnormalities and we published some very important papers related to that.

We worked with Dr. Jay Seegmiller who was one of the pioneers of treatment of uric acid diseases like gout. We interacted with a large number of people because of the nature of what we were doing and how we could collaborate. In other words, that's really what research is all about. It's not necessarily about what an individual does, but about how one can create a collaborative effort so that you have a lot of expertise focused on the same problem, and that's really the way the Clinical Center facilitates research in such an important way. You've got all these people who work in different areas, but when they come together it is really a force that's much greater than any individual.

KD: It sounds like some of the initiatives you talked about are things that came out of routine visits to the Clinical Center, observing people and deciding to go after some of those things.

PG: A lot of it is that and a lot of is that you have to establish certain types of research interests. Now physicians all over the country or nurse practitioners can refer patients to the NIH because they know you have an interest in studying a certain disease. This is the way things go on for the most part now. But in the early days we were dealing with descriptive things. We couldn't really advertise for them because we didn't know what we were advertising for. But we would see these very unusual problems, and this is how the program that we still are doing now evolved. We evolved a program of studying rare diseases, which gave us a particular opportunity to describe hormone action and these other things that I've mentioned before. But it also gave us a venue into taking on new technologies that would subsequently become available and how they could be applied to these clinical circumstances that we had created in the earlier period. Then I was ready to venture abroad by this time. We had reached a kind of mature state here and thought maybe that would be a good idea.

KD: How did that come about? Did somebody mention you might want to go look at Geneva for a few years?

PG: Vivian and I and our two sons were ready for a new venture. It turns out that I knew a cell biologist in Geneva by the name of Lelio Orci who had established a cell biology program in Geneva at the University of Geneva. So I met with Lelio and told him I'd like to come for year. He said, "You clinicians really don't know much about this." I said, "I know, but I want to learn." And he was very kind and let me come to the lab. There was a young Fellow in the lab who had been there for a couple of years, the only M.D. in the lab, named Jean-Louis Carpentier and he said, "I want to work with you." I said, "I don't know anything about what I'm doing." He said, "It doesn't matter. I want to work with you anyway." So the idea we had was to try to understand from a morphological visual point of view what was happening when a hormone bound to a cell, the work that had been created already within the Intramural Program.

KD: What Jesse Roth was looking at?

PG: That's what Jesse Roth and Ira Pastan, and Bob Lefkowitz had done. We wanted to see if we could actually visualize what they had done in a test tube. What would happen if we could visualize? Would we develop a new concept? After a while we were able to establish a visual image of a hormone binding to a cell, and we observed the fact that the hormone was taken up by the cell by a process called endocytosis, which means the hormone was being internalized by the cell. And this actually explained a phenomenon that we had developed before in the laboratory that is so-called down regulation, hormone receptors could be regulated up and down. And this explained how this process could go on, this process of endocytosis. It also explained how you could internalize a hormone and degrade it, so that you could shut off the signal. This really became a very important nuance.

The other interesting part of it was we were trying to develop the technology, and this was difficult because it was different from what Orci and the group had worked on before. It turns out that our former Fellows, Mike Brown and Joe Goldstein who were in Dallas, were working on a process similar to this with their low-density lipoprotein. So I contacted them and said, "Would you fix some cells in a particular way and send them to

us." And they said okay, and they did, and we reproduced with our system what they had done with their system.

Then I had a former assistant professor at Vanderbilt named Stanley Cohen. He was working with something called epidermal growth factor, which turns out to be an extremely important growth factor now, a number of cancer drugs had been developed related to that. He agreed that he would send us some samples. So now we were able to confirm what we were actually doing in Geneva by these networking sorts of things with these two different investigators.

Then I had the idea, why don't we put all this together and I found that they totally balked at this, and I couldn't understand why they balked at doing this collaborative research since we worked with them. I was too naive to understand that they were expecting to win the Nobel Prize, which happened in 1985. Brown and Goldstein won the Nobel Prize for LDL research, in 1986, Stanley Cohen won the Nobel Prize for epidermal growth factor research, and they were a little bit concerned about collaborating with each other. I realized that only later, but it was very nice. We had this wonderful paper published just before they won the prize, after I finally got them together. So it was part of my persuasion technology. I had learned how to persuade some of these people to do some of the things that we needed to do, and I was successful at that point.

KD: By the time they had done the paper they probably figured things were going to work out.

PG: It was okay by that time. I think it had gone far enough that it was okay.

KD: You talk about a technology you're using to do this imaging. What is that exactly?

PG: Basically it's the use of electron microscopy, so we can image things at a much finer resolution. So we could actually label a hormone and study it by autoradiography, which is making an image of where the radioactive material is going. We worked out techniques that we can show that was either on the cell surface or in some sort of internal organelle,

or whatever. The other investigators had worked out similar kinds of things for other hormones and this is how we were trying to put all this together to make it work for the system that we were working with. We did it basically with insulin and that was the initial study, and this gave us a lot of information about how insulin worked.

At the time we had the good fortune of having Ron Kahn still here at the NIH who could send us samples that we were studying under the microscope where he could do the kind of experiments that they were doing at the NIH lab, and we could work back and forth. This is something that fortunately we were able to continue over the years.

In fact, I have three Deans to my credit. When I say credit, I never thought I was really a mentor because these people were all so incredibly capable. It was just a very light touch. I had the chance to appoint Allen Spiegel, a Fellow, as Scientific Director who later became the Dean at Albert Einstein, and Jean-Louis Carpentier, who was the Fellow that worked with me in Geneva became the Dean of the Faculty based on the work that we had done. This is what propelled his career. And Jeffrey Flier who was working as a Fellow became the Dean of the Harvard Medical School. So I, perhaps not appropriately, take credit for the careers of three Deans at that point and that's also very special.

Because of the success of this work, and it turned out to be completely novel, we were writing papers as fast as we could, we were giving talks everywhere, I ended up staying a second year in Geneva, which was unusual. We spent the two years and it was fantastic. Then I came back in 1978. I came back as Clinical Director and so I was Clinical Director again doing many of the same kinds of things that I had done before.

KD: Had things changed over the last two years as far as the capabilities and the demands on the Clinical Director?

PG: I think now this new building, the glass box, had been erected. So the Clinical Center was expanding. Clinical research was expanding at the Clinical Center and the facilities for doing clinical research had begun to expand, so there was much more opportunity now to

do clinical research than there had been in previous times. A lot of this depends on the development of technology. The Clinical Center is in a unique position to assemble technology. And perhaps more importantly to assemble the individuals who could use that technology. That's really the bottom line of all of this; assembling the two things, having the source and having the people.

KD: Did you make decisions as far as you who you would bring into in the clinical area?

PG: Not so much make decisions. At NIDDK much of that is done by the Scientific Director, done by a process by either Clinical Associates or Medical Staff Fellows, whatever term we were using at the time. But managing the clinical program in terms of its safety, but in terms of also the kinds of imaginative or nuanced things it was involved in. The Clinical Director is more at that level than they are of formulating policy or those kinds of things. This is much more at the level of Scientific Director. I'm always involved in some sort of way, but not directly involved.

KD: Were you involved with Clinical Directors from other Institutes?

PG: Yes. We met on a regular basis. This is established Clinical Center policy. A lot of it was aimed at safety, a lot of it was aimed at technical development, a lot of it was aimed at what do we need to make this a better place and so forth. So you met with all the Clinical Directors on a very regular basis.

KD: Was this a heavy administrative lift? Were you getting to a point where you were doing administrative work as much as science?

PG: It is to some extent, but it sort of blends. I think that somehow the Clinical Center or the clinical research in the Intramural program has a certain kind of phenomenology that allows you to interact. In fact things are very physically close to each other. A lot of it has to do with how far away you have to go to be in the lab or the clinic, or some administrative function. One of the beauties of the Clinical Center is that many of these

things are close to each other. So yes, there are administrative responsibilities, but they're not overwhelming and I think it doesn't keep you away from participating in the scientific program.

KD: Are there any things that we should talk about in the clinical or scientific area before we move to the Directorship discussion?

PG: I think that the main thing is the growth of the Clinical Center. I always tried to play a major role because I felt the Clinical Center was a national institution and it was something that was going to help in so many ways. And the idea of, to some extent, partially leaving it was a difficult thing to do. We started to get to the next chapter where I moved not too far down the street, but it was an entirely new kind of experience as Director at NIDDK.

Jim Wyngarden who was the Director of NIH, in 1986, asked me to take on that responsibility. And I was reluctant to leave the Intramural Program because I had grown up in it and I felt a part of it. But I felt maybe I can make some new contribution and it would be a bit of a new turn, new twist on things. This is again a new learning experience. I think all these things, at least for me, have been new learning experiences, and that's what is really exciting about them because they're all new.

The Directorship is an entirely different kind of position and you realize you have a responsibility to a much larger community, this whole extramural community, as well as the intramural community. And you realize that either good times or bad times you have the same responsibility to sustain this incredible program which is going on and you realize that one of the key issues that sustains that program is budget. We have such incredible talent seeking resources to do such important things and everyone is looking to the Institute to support that. Unfortunately, we had some times where our budget literally was negative. Negative in the sense of so-called constant dollars in which when we corrected the budget growth that we were getting for inflation, the budget actually went negative, and that translated to what was happening with all of our investigators.

KD: Was this the case early on? When you came in did Jim Wyngarden have a policy change? Did he want a strategic change? What was going on at that point?

PG: I think that there was always an attempt to maintain the Institute as some sort of constant growth. That didn't always happen. Some Institutes got a greater appropriation. But this really all had to do with your relationship with the Congress because now all Institutes remember are autonomous and the budgets and the appropriations go to Institutes. NIH for all practical purposes doesn't have an appropriation. It does to some extent, but the majority of the budget goes to each Institute. And we actually were the fifth largest of the Institutes in terms of budget, so that is a very significant thing. And we struggled with that, and we struggled with trying to maintain all these interest groups.

We support over 50 interest groups and what they believe in. Sometimes they all want to work together, and of course your job is to try to keep them working together as a whole, but individuals obviously are greater proponents of their own interests than they are for the whole. And one of the jobs of the Institute Director is to try to maintain some kind of balance. And for an Institute like NIDDK that is a little bit more of an issue because we're divided into diabetes, digestive, kidney diseases, and all these areas, and it's very important that we maintain the strength of all these components.

Ideally, what you want to do is support the very best science that's out there. That's how the whole NIH peer review system is set up. So you have that system to guide you, but it doesn't necessarily solve the needs of all the individual groups. So everyone has a need. The drive is going towards the very best science that you can do. But you have to create some kind of a blend to make this work. This is I think probably one of the most important challenges an Institute Director has, first of all acquiring the resources and then figuring out some really equitable way for those resources to be distributed, always keeping in mind that the quality of science is what's really important, but also remembering that each of these components really has to be sustained, and it's very

important as to how they come together. That's I think a part of the challenge of the whole thing.

At NIDDK we have some fantastic people. One of the enormous resources we have is the quality of people, not only the scientists in the Intramural Program, but all of the people who work on grants, who administer grants who help maintain this whole community that we've developed through thick and thin. It's really up to the staff of the Institute to sustain them particularly through difficult times. When everything is really great it's not so difficult, but that's not always the case.

Fortunately, I was able to participate in the doubling of the NIH budget, which is something that came along some time later, and that was a great boon for NIH. It really, I think, represented a quality that NIH brought to the nation because you don't just double the budget without really having something to show for it, and I think that was the appreciation.

One of the things NIH has always been is bipartisan. So it's never really gotten caught in this somewhat vicious partisan divide that can happen. Both sides of the aisle, I think, have supported biomedical research because it's obviously in the human and the common interest. There are certain tangential areas that have become somewhat controversial, but that's not the biggest picture that goes on. The big picture is bipartisan and supportive.

KD: You would come in as Director in the Reagan Administration?

PG: Yes.

KD: So that's a period where there's talk about fiscal discipline and keeping budgets low, and things like that. Were you seeing a tendency to want to keep the lid on things during those first years?

PG: That was the point that made it so difficult because those were also high inflation years, and biomedical inflation is much greater than the standard inflation. So you had a much greater issue to deal with at that time. This is I think one of the real challenges, getting your community through this because there is another side, and the other side is when the NIH budget doubled. It's almost like crossing the Jordan River. There's another side. I wish I could sing gospel songs. Maybe I could have been more effective, but that's in some ways what you're doing.

KD: Did you have meetings and tell people this is what we have to do this year, but there's always next year and we're looking at these plans going out? How did you keep people moving along during that period?

PG: I think it's difficult to explain to someone why you're reducing their grant by 15 percent and now next year come back and explain to them you're reducing it by 20 percent. What are you doing that for? Remember NIH grants are given for several years and the out year costs have to deal with an individual appropriation year. So if the appropriation year doesn't account for what you spent the first year the only thing you can do is reduce it. The first thing you try to do is get people to understand that process and understand that you're going to do everything possible to reverse that, and you're going to do everything you can to help bridge them from one place to another.

There were so many people that were so grateful for what you can do individually to help bridge them from one difficult spot to the next, because again, there's always this upside that we're looking forward to and fortunately we have examples of this upside, so when you can point to these it's helpful. There's no magic way to deal with a downsizing economy, not just at NIH, but everywhere. It's one of the real factors.

KD: So one hand you're communicating with the scientists and lab Directors about appropriations. On the other hand you're communicating with the appropriators. Did you testify in Congress?

PG: Yes. Again, I found this natural. At first, I was a bit apprehensive about these kinds of things since all of a sudden now you're going up to a major congressional committee. When I first started, we were testifying for two hours in the House and for at least an hour individually in the Senate. I actually became very comfortable with that because I thought I was representing something that was important. They seemed to have an interest in it, and it seemed to go quite well.

Some of the things that you think might not be as pleasurable, particularly in this job, you do have to be very well prepared. This is one of the things that I was accustomed to. I had some terrific people who helped me prepare for congressional hearings. We worked very hard to portray the very best of NIDDK and the very best of NIH, because that's really a key part of what an Institute Director essentially has to do. As I said, when the budgets work, everything else seems to work much better. When they don't work it creates a much bigger struggle to sustain from one point to the next. The only way that you really do this is to know that there is another side of the river. It's going to get better and it's not all that different from talking to a patient about an illness.

You've got to try to convey an understanding and you've got to try to convey some sort of feeling. When things are either good or bad no matter what they are you have to be able to convey a certain confidence to the individual. In some ways my experience interacting with patients, something that I had done all my life, and something that I felt comfortable in doing really was the model for me, the model of what I was doing when I was testifying to Congress because it's really all part and parcel the same thing.

KD: Do you have any memorable occasions when you were speaking to Congress about things at NIH?

PG: I had a few ruts in the road occasionally, but most of the time it went fairly well. As time went on the Congress, the Congressional committees spent less time with the individual appropriations. We had a number of celebrities. For instance, I would testify with Mary Tyler Moore. We also had this major group, the Juvenile Diabetes Foundation, which she

was representing. Woody Johnson who is now the U.S. Ambassador to England was part of this. We had a number of other celebrity types and we would testify. There were also special hearings that weren't appropriations hearings that we participated in. Our Senator from Maine had brought a group of children in and she would ask the Institute Directors to come in and talk about diabetes and what they were doing for diabetes. And these were children, this was something the Juvenile Diabetes Foundation had sponsored and had gotten approval and permission to do. So you always ended up with certain other celebrity types in doing this. This was the way congressional hearings frequently go in that particular direction to influence in the moment.

One of the issues was so-called earmarking where individual groups would press the Congress for appropriations and the Congress decided they didn't want to deal with that. They wanted NIH to deal with that. So now in the latter part of the time I was Director, much of this earmarking phenomenon that the Congress had assumed before now was transferred to NIH. So now you had even more pressure. In our Institute we have over 50 individual interest groups. Our goal was to try to keep them as positive as we could as a collective group because we thought they could have a much greater influence than if everybody went off on their own. But that could only work up to a certain point, so you have to accept both sides of that.

KD: You talked about the situation you were in where you have to tell people there are going to be better days, and at some point there are. Tell me about that. What was going on that brought about the increase in budget at the NIH and how did you respond?

PG: I think in many ways the two people who were probably the most responsible for that phenomenon were the Director of NIH, who happened to be Harold Varmus at the time, and John Porter, who was Chairman of the House Appropriations Committee. Remember all appropriations bills start in the House and frequently that's one of the most important people, the Chairman of the House Appropriations Committee. I think it was really John Porter and Harold Varmus who probably played the pivotal role in developing that. We also had a lot of others; I go back to Warren Grant Magnuson and Mark Hatfield. All

these people were very important in terms of the growth of the NIH. They were all interested in the NIH. I think whether they happened to sit on one side of the aisle or the other was not the critical issue. The issue was the Institution and I think that's one of its strong points.

KD: Other strong points, we haven't talked about some of the big clinical trials, and those must have been of particular interest to you given your clinical background, the Diabetes Control and Complications Trial, for example, one of the biggest things happening.

PG: I think as clinical trials had evolved in hypertension, in lipid metabolism where we now had drugs and we now were making major impact in control of some of the most important chronic diseases it hadn't happened in diabetes. The Diabetes Control and Complications Trial was the pivotal primary trial that showed that even small changes in the average blood glucose could cause a major improvement, could lead to a major improvement in outcome in Type 1 diabetics, and that was really the key. Then we were able to get into a diabetes prevention program to try to add another step, and that was in Type 2 diabetes, a very successful program and still going on. We tried it in Type 1 diabetes to prevent it. That was not so successful. We've tried it in obesity, the so-called Look Ahead Program.

The important thing is that actually the clinical trials program really became very mature in our Institute for the first time because major clinical trials had really not been undertaken before. They had been small in certain ways, but not to this magnitude. And they were coming up in each of our divisions. We had attempts to control blood pressure to prevent renal disease. We had the trials for nutritional issues to try to control obesity. We had now a set of new Centers that were being introduced to try to bridge areas that didn't have quite as strong a research background as others. Sometimes the Center is a way to bridge that gap. It creates a funding stream. It allows an institution now to try to bring together an important research effort.

So in areas where research is actually very weak this is just as much a responsibility as an Institute has. You've got to somehow not just take those individuals who are excelling and whose grants and whose programs go, but try to find ways to augment those programs that are not, because the issues that affect the public are the same for those diseases in which progress is not as great as in those diseases where progress is much greater. So that's all part and parcel of the same thing. And you have to use different mechanisms. We established Clinical Nutrition Research Centers to try to bolster nutrition research. In fact, there were certain discoveries that took place. One that we can mention later, discover of leptin for instance, is something that has played an important part intramurally, but that also had a huge effect on funding the nutrition research because it all of a sudden created a whole new neural biology research program that we didn't have before.

All these things interact. They all become part and parcel of the growth of the Institute and you have to try and find a way to extend those things. Once you see a good example you've got to try to find a way to extend it, and that's really part of what the challenge is all about. It is trying to make it a broad based, rather than a narrowly focused, issue.

KD: So the Centers and these big clinical trials are a way to do that?

PG: Yes. I think the Centers and the big clinical trials are something that can be inaugurated only by the Institute. It's very different from so-called investigator-initiated research. It's not that you don't have advice from many people as to how to do these large programs. You do. But it's not the same as the classic NIH peer review program where an individual investigator is applying for a grant. This is a much more focused kind of thing. This has got to be an Institute effort that's coming from the Institute, from the staff of the Institute with all the advice that you can possibly bring to bear. You obviously want to get everything you can that's going to be positive about that to bring to bear on the issue.

KD: Any other highlights from your time as Director that we should talk about?

PG: There were so many things that we went through, funding in good times and bad times. I think that just working with the people that I had a chance to work with in the Extramural Staff Program, to learn much more about the Extramural Program to get much closer in a whole variety of diverse areas. You have diabetes, you have kidney disease, you have digestive diseases. You begin to interact and learn more about all these areas which I felt, again, because of the background that I had had, this broad background in clinical medicine, I felt very comfortable in these areas. But now you're really exposed, and it was a whole new learning experience.

Again, the congressional interaction, the NIH interaction, you're interacting with a pretty high-powered group of people just within the NIH community itself. To some extent you're competing a little bit. I think more we work together than we compete, but there's always a little bit of both. There are always certain kinds of friction that come up with these sorts of things. Everyone would like to be more of the recipient than the donor, which is what frequently these things come down to because there's always a pressure for Institutes to co-fund or to fund certain kinds of things. These pressures are coming from multiple places. They may come from Congress, they may come from the NIH Director, they may come from other sources, and you just have to deal with all of these different areas as they come up.

KD: Talk about the decision to head back to the lab and to step down as Director and go back to the bench so to speak.

PG: I think that first of all I had been Director for 13 years now and I think a kind of new revival and freshness is always a good thing for an Institute. I felt that we had by this time a billion-dollar budget, that we had done pretty well in the budget area. We had a very mature clinical research program. The basic research was going well, and my actual home was the Intramural Program from the very beginning. So here was a chance to go back and see what could happen.

We had the good fortune, a discovery that had just been made through an extramural grant to Jeff Friedman of this hormone called leptin. We then were with some intramural collaborators able to put together a whole program of research using these model systems that we had developed back in the early days. We studied these rare diseases like lipodystrophy, insulin receptor mutations, genetic diseases. This is what we had created and studied from the beginning. Now we had an opportunity to take the next step, that is the treatment of these diseases. We had described them, we recognized them, but we didn't treat them. Now we could do it.

So leptin then became a mainstay in treatment in lipodystrophy. We actually were able to get it approved in the United States for a generalized form of lipodystrophy and it's now been approved in Japan and in Europe for all forms of lipodystrophy. And we now have been able to establish an organized treatment program for one of these auto antibody syndromes that has to do with severe insulin resistance and we're working on how to treat patients with these genetic forms. It's a little bit more difficult. Our new investigator Rebecca Brown who's worked with me over the last several years has taken a major leadership role in developing therapeutic programs for those particular entities. That's really what the enormous opportunity has been. Much of it depends on the opportunity that you have.

I have been extremely fortunate in what I've been able to do within the NIH community. I spent time in Europe, with the Intramural Program, the Extramural Program and so forth, so it's been quite an experience. I have two sons, one is a professor of surgery at Vanderbilt, in a liver transplant program that interacts with the NIH, another who is an interventional pulmonologist in Seattle, a Center Director and we have a daughter-in-law who is an internist. We have our own HMO so we can continue this medical venture both within the NIH and outside of the NIH. So it's been a total pleasure over all these years.

KD: And we're back here in the Clinical Center, so you're clearly somewhere that's comfortable.

PG: Back home, exactly.

KD: Thank you very much for talking with me. It's been a great interview.

PG: It's my pleasure.