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SELNA L. KAPLAN, MD, PhD

Interview conducted by
Adolph Friedman, MD
January 10, 2000

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Dr. Friedman: This is Dr. Adolph Friedman interviewing Dr. Kaplan in her office on January 10, 2000, in San Francisco. Dr. Kaplan, do I have your permission to do this?

Dr. Kaplan: Yes, you do.

EARLY EDUCATION

Dr. Friedman: Thank you. Dr. Kaplan, I know that you were born in New York City on April 8, 1927. Would you be kind enough to tell me a little bit about your earlier education? When you went to high school, did you do anything of any special interest in high school? Were you interested in music or art? Did you excel in anything? Were you an athlete?

Growing penicillin at Midwood High

Dr. Kaplan: I went to Midwood High School, which was a new high school that had just been open for a few years; and I had an interest in science at that time and actually had an elective that I did with one of the biology teachers--interestingly enough--on growing penicillin. We had mold and special jars in which to grow it--and injected it with the mold and grew a little penicillin, not enough to do anything with. But I had the experience of doing that, and I really enjoyed those experiments and other things that we did related to science. And actually I won the medal for biology in high school, probably because of that interest.

BROOKLYN COLLEGE: A CONTINUING INTEREST IN BIOLOGY

Dr. Friedman: No. I think it's because of your accomplishment, not because of your interest.

Dr. Kaplan: At any rate, so that was. I had no contact. No one in my family was in either science or medicine and at that time and, so it was only my own interest and, of course, the encouragement of the teachers in school that lead me along to this path. Then I went to Brooklyn College, which is actually practically across from the street from this high school, and continued my interest in biology there--in terms of not any really experiments, just the usual courses that I took in biology, but there was no one there who had any special programs of research, at least none that I got involved in as I recall. My memory is a little thin, but I don't remember that at all until I went to medical school.

WASHINGTON UNIVERSITY

Deciding on a PhD in anatomy rather than an MD; on being female, Jewish, and a graduate of a city college; research on skin cancer

Dr. Friedman: Before medical school?

Dr. Kaplan: Yes. Actually, after Brooklyn College--or while I was in the last year at Brooklyn College--I took some special courses in microbiology and in microscopic anatomy and decided

to go for a PhD. Primarily I chose that because I was told by my advisor in college that I had three strikes against me before my grades were looked at; that is, I was a female, I went to a city college, and I was Jewish. And no matter what my grades were, I would have a hard time getting into medical school. So I decided to go to graduate school, and I went to Washington University in St. Louis and started my training--actually in the anatomy department. And the anatomy department at that time was doing some cancer research on skin abnormalities, and so I did some studies for my master's degree on methylcholanthrene effects on skin and did some biochemical analyses of the skin.

Dr. Friedman: Would you mind spelling that methyl term?

Dr. Kaplan: M-e-t-h-y-l-c-h-o-l-a-n-t-h-r-e-n-e. I think that's correct.

Dr. Friedman: Thank you.

PhD thesis: vitamin-E abnormalities in pregnant rat; deciding on medical school

Dr. Kaplan: And then went on to my PhD thesis, which was on vitamin-E abnormalities in pregnant rats, and I looked at the fetal tissues, the tissues of the mother, and made about a couple of thousand slides--since that was the limitation--they were dye studies since we didn't have electromicroscopy, yet, or any other types of analyses to be done--and I received my PhD degree. However, during my last year of the PhD, I decided--because I had taken courses with medical students--that they seemed no smarter than I was. So I decided to apply to medical school--one time. If I didn't get in, I would continue with my doctorate studies. Actually, I only received applications from four of the twenty schools I wrote to, and the only one that granted me an interview was Washington University, and they accepted me after an interesting conversation with the committee.

Dr. Friedman: I can see that you are fortunate to get into such a good school.

WASHINGTON UNIVERSITY MEDICAL SCHOOL

Research in microbiology

Dr. Kaplan: Yes, I really feel that it was very fortunate, and I was pleased with that. I did do some research in microbiology while I was in medical school, but they--since I had taken all the first year courses--and what I wanted to do was move along and be given the opportunity to take off a year and do more research, but they wouldn't agree to that. So it was a consequence that [I] was matriculating and looking for a job, and, fortunately, I was able to replace one of the instructors or professors of anatomy, who was going to identify war dead. I don't know which war it was--Korean War, perhaps. I've forgotten. This was in 1950.

Dr. Friedman: Fifty-four or fifty-five--in the fifties.

Teaching anatomy while a first-year medical school student; research on viral injections into the brains of mice

Dr. Kaplan: Well, when I was in my first year of medical school, so that would have been '51. I don't remember exactly what war it was, but she was an expert in identifying soldiers from their bones--length and height and so forth. So they then allowed me--to agree to appoint me as instructor in anatomy, gross anatomy. I actually was the instructor for my own classmates--who didn't realize I was in their class because I never-- [phone interruption] --during the first year. So the money I received equaled the money that I would have to pay for matriculating. So we had that deal. And during that time--since I wasn't taking any classes but just teaching--I was able to complete my thesis and present it for my final exam. Then the second year, I joined my classmates and went on to do some research in the second year with one of the professors in microbiology--injecting some viral solutions into the brains of mice to see what the effects were.

PEDIATRIC TRAINING: BELLEVUE HOSPITAL INTERNSHIP; KINGS COUNTY HOSPITAL

Deciding on endocrinology

So that was part of my research and some other things that I did then. Then when I graduated from medical school in 1955, I decided to go back to New York, and I interned at Bellevue Hospital and then went on to complete my pediatric training at Kings County Hospital, which is as large--in a similar city--hospital as Bellevue, not as well known, but still the same types of patients and activity. It was during that time that I started to think about what I wanted to do when I completed my pediatric training. I decided on endocrinology since I had an interest in biochemistry and also in pediatric patients and felt that endocrinology would be the specialty that would satisfy my interest.

Choosing pediatrics

Dr. Friedman: I have two questions: One, what stimulated your interest in pediatrics or steered you toward pediatrics? And the other thing was, during your resident season fellowships, did you have any professional contact with any famous people who subsequently influenced your career?

MEETING MELVIN GRUMBACH

Dr. Kaplan: Well, in Bellevue, I didn't--although, the head of the department then was a notable pediatrician, Dr. [Luther] Holt, who was a notable professor of pediatrics. But the main influence in terms of pediatrics--I think in medical school I'd found that that was the area that interested me most. I really didn't feel drawn to taking care of adults or older individuals, and pediatrics was the area that appealed to me most--in terms of dealing with the children of the families. I enjoyed that mostly, more than anything. When I was at Kings County, Dr. Dick Day, who is a notable neonatologist and, actually, is still in practice here in California--I expressed to him my interest in terms of biochemistry and such, and he discussed with me

potential approaches to this and encouraged me to take a fellowship. He gave me the names of several people, including that of Dr. Grumbach, who had just moved from Baltimore, Johns Hopkins--where he took his training--to Columbia University, where he had been a medical student. So, I interviewed with Grumbach and then started my fellowship with Dr. Grumbach when I completed my pediatric training, which was the end of June 1958. I started with Dr. Grumbach in July of '58, and we quickly decided that we work well together and just continued.

FAMILY BACKGROUND

Dr. Friedman: I have a couple other questions, which I'd let go by because you are speaking so fluently. Where were your parents born? Did your parents have any education? Did they have any professional accomplishments? Did they progress that far?

Dr. Kaplan: My parents were born in Lithuania. My father came when he was thirteen; my mother, when she was sixteen. My parents were first cousins, and they had limited education. My father probably had more because he was a male and had more education, more in the religious education. My mother had limited education, although she was a very bright woman and learned to read quickly--read English quickly--as did my father. They had eventually a mom-and-pop grocery store, but initially they worked in factories and did that type of work for a while until they decided to do the final thing that they did--for probably twenty-five years of their lives--and that is, had a mom-and-pop grocery store. So they had limited education. I would say neither of them went to high school. They went to part of grade school. It's a little hard for me to know exactly what--how much they did in Europe compared to the limited amount they did in the United States at the time that they came. But they both liked to read a lot and encouraged me to read and encouraged me in everything I wanted to do. They were very supportive throughout all the changes that I made in my life--going away out of the State to graduate school and then to medical school. They were fully supportive for whatever I wanted to do, and that was very helpful.

Dr. Friedman: Did you have any siblings?

Dr. Kaplan: I had a younger sibling who died when I was about four years old. She died of erysipelas because there were no antibiotics at the time. That's the only sibling I had. So I was an only child for most of my life.

Dr. Friedman: Have you ever had any children?

Dr. Kaplan: No.

MOVING TO CALIFORNIA TO WORK WITH GRUMBACH

Dr. Friedman: Once you got involved with Dr. Grumbach, you continued with him, and then you moved to California. Did you go to California because it was related to your pituitary and

gross hormone work, or did you go to California because he went and you worked so well together?

Developing new methods to measure growth hormone; working with Berson and Yalow

Dr. Kaplan: Well, I would say that it's primarily two things, not the one you mentioned. One is that, having had prior visits while I was in medical school to San Francisco, I really fell in love with San Francisco and sort of had a promise to myself that one day I would live there. When this opportunity arose and Dr. Grumbach asked me to come along, I thought that this was a great opportunity and this would allow me to be in charge of the endocrine group because he was going to be busy with being chairman. So it provided me with an opportunity to extend the research that I had already started in New York, which was working on a variety of new methods to measure growth hormone. I had the opportunity in New York after a fiasco with a method that used hemalile cells--read method--which didn't work well, which I determined from my studies. I linked up with Berson and Yalow--Berson was a friend of Dr. Grumbach--and the Berson and Yalow team was in the Bronx, which is not too far from where Columbia was. Because we provided them with some purified growth hormone and antiserum, which I had made for my other studies, they allowed me to come in the lab while they were developing their assay and learn the assay from Roth and Glick, who were fellows then with Berson and Yalow. So that was my introduction to the radioimmunoassay--I had been working on with other hormones--so [I] became familiar and then carried it on in our own laboratories, eventually, and started to test the children. So we had done the testing, but hadn't completed the measurements, and we transferred seven freezers of samples from New York to San Francisco.

SETTING UP A LABORATORY AT UCSF

Dr. Friedman: That was a project.

Dr. Kaplan: Yes, it was because we had to pack them in dry ice and have them shipped from there. I went to San Francisco three months later, and Dr. Grumbach left the end of December of 1965. I left in March of 1966 to come to San Francisco because I had to get all the samples packed up and all the equipment shipped. We had a beta counter to ship--and all the other supplies that we had to ship that we were using at that time. So it was the "flying tigers" with an airline that moved all the materials--at least the frozen materials--to here, where Dr. Grumbach had to find freezer space before our freezers arrived from New York to San Francisco. It was quite an experience to pack it up and get it here. When I arrived, the laboratories that we expected to go to had not been completed. There were new laboratories--new research buildings that were completed by July of that year--and so we had to stay in some temporary facility with all of the packed equipment, although we got all the samples into freezers right away.

Dr. Friedman: That was very fortunate.

Dr. Kaplan: Yes. It was an interesting experience, and then I set up the clinics and started to talk to physicians in the area--I started to talk to the patients--and they lined up a number of patients for us to test, and so I had to go through all the charts and decide who would have to be

tested and so forth. It was a very busy time the first few years that I was there. Then, the following year, we had the first arrival of our fellows who came. We had many fellows from the United States and from Europe who came in the first group to study with us, who have made important contributions of their own to pediatric endocrinology.

DESIGNING THE FIRST RADIOIMMUNOASSAY FOR THE DIFFERENTIATION OF GROWTH HORMONE

Dr. Friedman: Were you and Dr. Grumbach the ones who differentiated placental chorionic somatomammotropin or growth hormone from pituitary growth hormone?

Dr. Kaplan: We set up the first radioimmunoassay for that, but it was someone in gynecology at another university who first identified the hormone, and then we became interested in that. I arranged to have to have the hormone purified. And when we had the purified hormone, I made antiserum; and we set up the first sensitive radioimmunoassay for that placental hormone and noted that it cross-reacted with growth hormone to impart, but the assay was able to distinguish between the two.

THE FELLOWS OF HER GROUP

Dr. Friedman: I was going over all your bibliography, and I had a couple of questions of who in your group was so fluent in French to enable you to publish your article in the [French] *Annals of Endocrinology*. Was it [Pierre] Sizonenko?

Dr. Kaplan: Sizonenko was from Paris. He originally had been in Paris and then moved to Geneva in Switzerland where he has recently retired, but he's still practicing pediatric endocrinology.

Dr. Friedman: What happened to 1970 and '77? He seemed to have disappeared from your bibliography?

SUPERVISORY RESPONSIBILITIES IN THE LAB

Dr. Kaplan: Well, he went back to Switzerland is what happened. So he was doing work there, and there was some communication that we had and did some work together, but basically he started to set up his own unit, primarily in Geneva, Switzerland, and did do some work and has published a great deal on his own, as well as Dr. William Burr, who worked as a fellow at the same time as Sizonenko. They did the extensive work on puberty that I had set up, which was based on other assays that had been set up by--I made the most of the antiserum that we used in our studies--both the first and second antibody--during the time that I was doing this work and analyzing them. So our fellows did the clinical studies that we developed, but I was the one who was in charge of the laboratory work, setting up the assays initially, and then overseeing the laboratory personnel as well as the fellows when they were in the immunoassay laboratory.

ON THE CONTROVERSIAL USE OF GROWTH HORMONE IN NON-GROWTH HORMONE DEPENDENT SHORT STATURE

Dr. Friedman: A few of your articles were on the effect of growth hormone in non-growth hormone dependent short stature. I was not aware that it worked.

Dr. Kaplan: This is--still after all these years--has been a constant battle as to the determination of whether it works or not. If one talks about it--work--yes, it does in the immediate time that it's first given. It does increase the growth rate. The point of contention is whether it has a beneficial effect on final height. This is still controversial, but most of us feel that the vast majority does not have a significant effect on final height. In studies recently done, which I collaborated with another group of pediatric endocrinologists [on] and [was] carried out by Genentech, there was an increase in final height of a limited degree, that is, about an inch or two, and that is after some six or seven years of growth hormone. So I don't consider that growth hormone [in] non-growth hormone deficient patients is useful other than having an immediate effect on growth. I think it has very limited effect on final height, if any, and I've been outspoken on this opinion at many meetings, although it's not always in finding agreement with everyone. There are still many who believe that it's useful that short children should be treated with growth hormone. I am very selective in terms of children who were not growth hormone deficient, but our criteria--and we've used more stringent criteria that have required a very low level of response to provocative stimuli--and so discontinues. There are still a lot of short children being treated with growth hormone, and I am not in agreement with that.

Dr. Friedman: What is the immediate effect?

Dr. Kaplan: The immediate effect is that in about seventy percent of the children one can see an acceleration growth rate--sometimes a doubling of a prior growth rate. So you can see an immediate effect of increasing their growth rate. In thirty percent we don't see any improvement in their rate of growth, and so that you have a situation: we don't know why those children have an improvement in their growth rate. We're giving them additional growth hormone, so that may lead to any state in which you double the amount of hormone. It may allow them to grow better, but it doesn't. There are other factors which affect whether it will induce an improvement in their final height; because puberty ensues and that may proceed at a faster rate than is normal, or there may be more of an advancement in the bone maturation, which also will have an adverse effect or not allow them to have an improved final height. So there are a variety of factors, and they are being explored now, and some of these are sorted out. Some of the children who are extremely short and not growing well may have some problem in processing a growth hormone--which I have suggested and others have suggested--but I haven't done the studies to demonstrate this. There are others who are doing those studies, now.

Dr. Friedman: Are you implying that the mass action--they have something to do with it by adding supplemental growth hormone?

Dr. Kaplan: Well, yes, if you want to look at it that way. Yes. We know that in situations where there is excessive secretion of growth hormone, as in acromegaly, if it occurs before bone

fusion--if it occurs in the younger child or adolescent--they will grow excessively, but that's even of a different magnitude than what we provide in injections. The amount that's secreted by the pituitary when there is a tumor is of much higher level than that which we administer by the daily injections. But, yes, it's a mass effect,. You give more--and the concern, of course, is how much you can give. I mean, you don't give as much as two weeks levels--as we see in gigantism--because there are other side effects that you don't want to induce such as glucose intolerance, some other effects on muscle mass, and so forth. So, you don't want to do that. You would like to keep within--without inducing adverse effects and just inducing beneficial effects. But I think that, for the most part, growth hormone administration is probably overused currently, and I am not in agreement with that.

COAUTHORS

Dr. Friedman: There are a lot of people who were amongst your coauthors that I didn't know, and amongst them, for example, was [Felix] Conte.

Dr. Kaplan: Dr. Conti actually is still with us. He is a clinical endocrinologist. He has been a collaborator. He does primarily clinical endocrinology. He's an exceptionally bright individual and has done a lot of work on ambiguity of sexual development, and he actually has written a chapter in Williams [Williams Textbook of Endocrinology] with Dr. Grumbach on sex differentiation, and that's his main area of interest. But also, since he's an endocrinologist, [he] sees a lot of patients, and so collaborates with us on all the clinical studies that we do.

Dr. Friedman: How about Sciarro?

Dr. Kaplan: He was a gynecologist who worked with us and then left; I don't remember where. He went to be chairman of [a] department of OB/GYN elsewhere, but we collaborated with him on some of the studies that we did, particularly on the placental hormone.

Dr. Friedman: Is there anything else I should know about Sizonenko?

Dr. Kaplan: No. Other than--in European pediatric terms--he's a very renowned pediatric endocrinologist, and he still continues to do clinical work, although in Europe you have to retire when you're sixty-five, which is not true in the United States.

Dr. Friedman: Fortunately.

Dr. Kaplan: So he has retired and he's still doing clinical work. He is no longer head of the unit at the Children's Hospital in Geneva.

Dr. Friedman: How about Aubert?

Dr. Kaplan: [Michael] Aubert is a PhD who has worked with us for several years in the laboratory doing some studies on prolactin and on structure of growth hormone with some of the people in C. H. Li's Laboratory. He's now on the faculty at Children's Hospital in Geneva,

Switzerland, and has continued to do work in rats on pubital development--on gonadal development of the rats--in looking at various abnormalities related to that lepton. He's looked at a variety of GnRH effects, and so forth. So he's continuing to do a lot of very notable work related to that and to nutritional status, and using the rat as the model. He's primarily a laboratory person.

Dr. Friedman: You mentioned C. H. Li. Have you and Dr. Li worked together very well?

Dr. Kaplan: Well, he provided us with some preparations, and we also did a couple of studies with him, not too many, since he had independent studies that he was doing, but we had several papers and studies that we did with him and worked with some of his trainees in his laboratory.

Dr. Friedman: How about Lovinger?

Dr. Kaplan: Robert Lovinger was a fellow of ours, and when he completed his work, he went to Virginia and has been in pediatric endocrinology, doing primarily clinical work and a lot of diabetes work.

Dr. Friedman: In practice or the university?

Dr. Kaplan: Well, he mostly was in practice. He had an appointment at the university, but he primarily was in practice.

Dr. Friedman: How about D. M. Styne?

Dr. Kaplan: Dennis Styne was someone who worked with us on a lot of the puberty studies, and actually he was here as an assistant professor, and then he was offered a position at the University of California, Davis. He moved there and eventually became chairman of the Department of Pediatrics at Davis--and has just resigned as the chief of pediatrics there and is now continuing to do pediatric endocrinology. He is chief of the Division of Pediatric Endocrinology. So he is at Davis and still continuing to do there, and he's also collaborated with Dr. Grumbach on writing a chapter on pubital development for the Williams text [Williams Textbook of Endocrinology].

Side A ends

Side B begins

Dr. Friedman: Go ahead. Were you still talking about Dr. Styne?

MORE ON SUPERVISORY RESPONSIBILITIES

Dr. Kaplan: No. I think that I was finished with Dr. Styne. I was just going to say--just in summary--that my responsibility with the fellows and with the clinical research was to teach the fellows the laboratory tests--the radioimmunoassay--[and] was to organize the clinical studies,

write the protocols, get the authorization from the FDA for using the new materials, and recruiting the patients. The fellows did the actual analysis of the data, but I was responsible for getting everything together and for going over the studies with them.

NATIONAL PITUITARY AGENCY

Studies of abnormalities being treated with growth hormone

Dr. Friedman: Another one--whose name I remember, but I hadn't had any contact with--is Dr. Raiti.

Dr. Kaplan: Sam Raiti was the chief of the [National] Pituitary Agency, and I was the chairman of the Committee on Growth Hormone of that agency for seven or eight years. That was during the time when we were providing pituitary growth hormone for patients, and we were required--in order to get growth hormone, the requirement was that studies had to be submitted and reviewed by our committee, and then decided whether we would provide the growth hormone for that study. There was no other source, initially--until probably the 1980s or--for any pituitary growth hormone. There was one company that started to provide commercial growth hormone for a while. In 1981, I was the principal investigator for the Genentech study, but before that time came up, I had worked closely with Dr. Raiti on organizing some studies and doing some national studies on certain of the abnormalities that were being treated with growth hormone--short stature, Turners [syndrome]. We did a lot of short-term studies on that that we wrote up. I was chairman of that committee that looked into the quality of materials that we were getting and helped to urge that we use more purified growth hormone as was being provided by Dr. [Albert] Parlow and also by others in the group--by Dr. [Alfred] Wilhelmi.

Dr. Friedman: I was going to ask you about Wilhelmi later.

Dr. Kaplan: Okay.

Dr. Friedman: How much contact did you have with people like Wilhelmi and Guillemin, on whom in your bibliography there are one or two articles, here and there. That was about it.

ALFRED WILHELMI AND ROGER GUILLEMIN

Dr. Kaplan: Wilhelmi I had a lot of contact with as chairman of the Committee on Growth Hormone because Wilhelmi was one of the major providers of purified growth hormone. He was one of the three or four biochemists who received the pituitaries, and then purified it, and provided us--the [National Pituitary] Agency--with the growth hormone that we then distributed to pediatric endocrinologists. So he was part of this committee that met regularly several times a year to discuss this. We had some discussions by phone, and I knew Al very well at meetings. So that was my contact with him. Roger Guillemin was at the Salk Institute in charge of the program there on peptides, and he purified a lot of the hypothalamic peptides, of which he was one of the people winning the Noble Prize for that. He was a friend, and he provided us with the purified peptides that he developed--hypothalamic peptide. He gave it to us to do the clinical studies in children, and he had collaborations with others who did the clinical studies in the

adults. So we were the first to have available to us varieties of the peptides: LRF (luteinizing hormone-releasing factor) and GRF (growth hormone-releasing factor) and some of the other peptides that we were able to use and carry out clinical studies in children--well ahead of others who later developed the peptides as well. He was a close collaborator, and I knew him well, also, when I was on the council of the Endocrine Society. He was president of the Society at that time, so I had close contact with him at the council meetings as well, but he was always available to talk to us about new peptides that he had and whether we would be interested in testing them and so forth. So he was a very close collaborator, and I still know him--see him at the meetings. I don't have other contacts with him, usually.

WILLIAM F. GANONG

Dr. Friedman: The next person that I was going to ask you about was Ganong.

Dr. Kaplan: Yes. Craig (??) [William F.] Ganong was chairman of the physiology department here, and I did attend his conferences for many years, and I did some collaborative work with him on some studies. We did some studies in the dog. He was using primarily dogs for most of his endocrine studies, and I collaborated with him and with his trainees. I helped with his trainees in terms of immunoassays and in terms of planning some studies that were done in the dog. He has continued to be a friend. He is retired now, but he still comes to conferences, and I still see him there. He worked with us for many years and was very helpful in some of the, primarily, dog studies that we did.

Dr. Friedman: Again, was this on pituitary gonadotropins?

MOST ENJOYABLE AREAS OF WORK: THE LAB, DEVELOPING ASSAYS, DOING CLINICAL RESEARCH AND FETAL ENDOCRINOLOGY

Dr. Kaplan: They were partly on that. Some of them were studies that he was doing on other peptides that he wanted to look at--other hormones--and how they affected--or lesioning of certain parts of the brain or the spinal column, which were some of the studies that he was doing and wanted to see how it affected other hormones. I was able to set up some assays for some of those hormones, which I did. We set up assays for dog growth hormone and dog prolactin. We did some of my own studies and did some studies with him, and he helped us with some of the studies we did in dogs. So that was our collaboration there. It was limited. But, you know, it's at different times. You know, you do one thing, one time, [and] then change over to other studies. We've worked with dogs; we've worked with sheep. You know you asked me what I enjoyed most. I think the two things I enjoyed the most--one thing I certainly enjoyed--I loved working in the lab. I like developing new assays. I like doing new methods, and I really enjoy not only supervising the task but actually doing the work myself. I don't know. It gave me a certain satisfaction to be able to do that, although I couldn't continue to do that. As my responsibilities increased I had to give up doing lab work, just could supervise it, design(??) it, and develop new assays, at least--that the technicians carried out. That's what I enjoyed doing. I also--from a point of view of the research, I would say, although I enjoyed the clinical research and still do that, my greatest enjoyment was the fetal endocrinology. I had a great interest in

that. We do a lot of work in those--primarily in the sheep. We started in the human--in autopsy specimens. But then when we came here to San Francisco and the cardiovascular group in pediatrics was using the sheep, we set up with them: to use sheep and catheterize the fetus in situ, to relieve the catheters in the fetus and bring them through the mother's belly, and then we could sample and test the fetus while the fetus was--

Dr. Friedman: That was fascinating.

Dr. Kaplan: Yes. So we did a lot of work on that in that we worked with--one of the fellows who came and worked with us was Dr. Peter Gluckman, who is from New Zealand. He was superb. He has gone back to New Zealand, and now he organized his own unit in the pediatric department there and then became dean of the school in Oakland. He has become very notable, in terms of having started with the studies with us, but has gone on to do a lot of independent work on using the fetal sheep as a model. That was a fascinating part of the work I did--in addition to the clinical endocrinology--but that was the most fascinating part of our work.

Dr. Friedman: Every time you devise a new assay--in its achievement and accomplishment--there is gratification in each stage of it.

Dr. Kaplan: Well, we developed the assay depending upon the circumstances. I mean, for example, we hadn't developed assays when we decided to use the sheep. We had to develop assays for those studies. I mean _____ growth hormone, prolactin, LH, FSH--those are all assays that we had to develop. We received antiserum for some of them, but for some of them we had to make our own antiserum, and then try to set up the assay. So, this was a challenge, but we had excellent trainees who came to work with us, and they were superb. And they've gone on to do things on their own, whether in clinical endocrinology or, as Dr. Gluckman--he stayed with the sheep studies, and he is really notable in this field and for all the work that he has done on his own. He has done a great deal of work and still--

Dr. Friedman: That's a tribute to you, also.

Dr. Kaplan: Yes, well, I think we--Dr. Grumbach and I--have had a fortunate time. We have had very good trainees who've come to work with us and then gone out on their own, and I would say [the] percentage is probably ninety percent of our trainees are still in academic medicine. They're both from those who were in Europe and the United States. So I think that's a record that we're very pleased with. We've at least encouraged them, inspired them to continue in the work, and they've continued to do it and are known for their work--and this continues. We continue to do that. That's also part of the work that I enjoy. I enjoy having all these trainees because you learn from them.

Dr. Friedman: Of course, and it's also gratifying to see them progress on their own.

Dr. Kaplan: That's right.

SUPPORTING FELLOWS

Dr. Friedman: How about Kelch?

Dr. Kaplan: Bob Kelch is the one who worked with us on some of the clinical work on pubertal hormones, and then he went back to the University of Michigan as chief of pediatric endocrinology there and continued to do excellent work and clinical studies there. Maybe about four years ago, he became dean at the University of Iowa, where he still continues. I don't think he's doing any endocrinology anymore, but he is dean of the medical school at Iowa. He's one who is a very bright, delightful person in whom I am still in contact with. I try to stay in contact with all our fellows, so that--Christmas is a good time to contact them--and I do that regularly for both the European and the US fellows. Part of having fellows is not only teaching them assays, teaching them how to do clinical research; it's also teaching them how to be good physicians and how to do their work properly, and keeping them from getting discouraged when things don't work well.

Dr. Friedman: We all need that sometimes.

Dr. Kaplan: So there is a lot of time that you just spend talking to people and keeping their spirits up--fellows particularly.

Dr. Friedman: How about Glen Sholene? Once or twice I saw his name. He didn't do much, apparently.

Dr. Kaplan: No. Well, he was a collaborator. He was, I believe, in radiology.

Dr. Friedman: How about C. H. Sklar?

Dr. Kaplan: Chuck Sklar is a fellow of ours who did some work in fetal endocrinology, which we had all the fellows try. He wasn't interested in that, and he switched to clinical endocrinology. He did very well and ultimately went to NYU in New York and became very interested in oncology and endocrinology--and is now in New York.

Dr. Friedman: We were talking about Sklar.

Dr. Kaplan: Chuck Sklar. Yes. He is now at Sloan-Kettering--involved with overseeing the pediatric endocrine group at Sloan-Kettering--and has made important contributions to the field of the effects of radiation and oncologic treatments on development of endocrine deficiencies and so forth.

Dr. Friedman: He didn't work on the adverse effects of radiation, did he?

Dr. Kaplan: He did work on that, yes. That's what he has been working on. We work with some others. Some other fellows were doing that initially, but he continued to do other work when he was at NYU and then went to Sloan-Kettering; so he has been working on that as well.

Dr. Friedman: Because Dr. David Becker and Jack Robinson at NIH have done a lot of this work on the adverse effects of radiation.

Dr. Kaplan: Yes. Chuck has done it primarily in pediatrics. That's where he has been working. It's not only that; he has been looking at chemotherapy and its effects--radiation and a lot of work on that. He has also done some thyroid abnormalities in children who have been irradiated.

Dr. Friedman: That's what Robinson and Becker have done. There was also a pathologist from Washington, who died a number of years ago--pediatric pathologist--who started the work on the fact that a child with cancer developed after radiation to the _____.

Dr. Kaplan: Yes, yes. I remember that.

Dr. Friedman: How about Schriock?

Dr. Kaplan: Elizabeth Schriock was a fellow with us and did work on GRF and some other studies. Her husband is a gynecologist, and he had a position offered to him in Memphis, Tennessee, so she moved there and was in charge of the pediatric endocrine group in Memphis. Her husband was offered a position back here, and she's now returned to this area. Because we didn't have an opening, she decided--she had a position running the peptide laboratory for the gynecology department/reproductive endocrine department, and she continued that until a couple of years ago. She then decided to [take] early retirement because she has three children, and they were getting of an age that she felt she needed to be more attentive to their needs, but she still attends our conferences, and so we're still in contact with her.

Dr. Friedman: Was [Aaron] Vinikone one of your fellows?

Dr. Kaplan: Yes. He came more as a visiting professor. It's hard to sort of make the classification--depending on how far along they are in their work. He came from South Africa and worked with us for a couple of years. He's now doing more diabetes work, which was a main interest of his. He is doing more work on diabetes and other pancreatic hormones. I don't remember where he is located now.

Dr. Friedman: I think it's North Carolina.

Dr. Kaplan: Yes. He's in the United States now.

Dr. Friedman: In one of the Carolinas.

Dr. Kaplan: Yes. We see him in meetings, but he was really an excellent person. It was unusual since he was an internist. We don't often have too many internists who spend time with us, but he was an internist.

Dr. Friedman: I will come back to the pediatrician. Was G. P. August--Gilbert August? He is

the one that worked with Wellington Hoang. He's retiring as of now, also.

Dr. Kaplan: Right. My fellows are retiring before I retire, but that's one of those things. Yes. A lot of our fellows have retired. [Howard] Kulin has retired, and some of the others are retiring.

Dr. Friedman: There was another one that I didn't understand in the bibliography, but I understand it now that you mention that you visited Berson and Yalow--was J. C. Roth. That's Jessie Roth?

Dr. Kaplan: That's Jessie Roth. Yes.

Dr. Friedman: I am in an interesting position at the moment. I was fortunate enough to be able to interview Rosalyn Yalow, and--before Jesse Roth and Glick--there was a fellow with the name of Rothschild and Arthur Bauman with Berson and Yalow.

Dr. Kaplan: I know Rothschild; Bauman I don't remember. Which Bauman?

Dr. Friedman: Arthur. He became a clinician. But the story was that--when you mentioned the spinal cord injury, I was waiting for an opportunity to introduce this point. Bauman's son, William Bauman who is a professor at Mount Sinai Hospital, has gotten involved in the last couple of years on endocrine abnormalities in spinal cord injury in paraplegics, and he is doing a tremendous amount of work all over the country, and he has a series of about twenty-five sets of twins, one of whom is a paraplegic, and one is so-called normal. He has been running parallel hormone _____ and evaluations on these groups. But, anyhow, I interviewed Arthur Bauman before he died. He was a close friend of mine. William Bauman got me in to see Yalow, and I have all of the documentation that's in print on Berson. And I recently met Rothschild at a social function in Florida, and I'm trying to convince him to send me his memorabilia and give me either write-up notes--like you and I are talking now--or to put it on tape, and I'll have it transcribed. But, he's not moving very rapidly. I'm hoping to correlate all of this and then interview Jesse Roth and put it altogether as one composite Berson and Yalow group.

Dr. Kaplan: Right.

Dr. Friedman: Where is Glick now?

Dr. Kaplan: Glick is in Israel.

Dr. Friedman: Well, that takes him off the list.

Dr. Kaplan: Glick moved to Israel. After his fellowship, he worked in Coney Island Hospital. He is very religious; he decided to move to Israel. I forget now exactly where he is--so that's where he is. I see him periodically. There is some medical ethics program that they run yearly in San Francisco, and he's coming for a few of those, but Jesse--Jesse I know very well, too.

Dr. Friedman: He moved again. He is now in Long Island.

Dr. Kaplan: He and Seymour [Jesse Roth??], as I said, were fellows when I learned immunoassay from them. The only reason he got into that laboratory was because Yalow had a rule about--I guess Berson did, too--about not letting anybody work in their lab who was not *in* their lab. You practically had to sign an agreement not to do anything without their permission--you know, publish anything without their permission.

Dr. Friedman: Roz Yalow, before she had a stroke, was a tough cookie.

Dr. Kaplan: Yes. That sums it up. I didn't know she had a stroke. At any rate, it was very enlightening to work in that lab. We were able to do it even though--Mel was a friend of Berson, but it's also because we gave them the antiserum that allowed them to move along faster in their developing the assay.

FETAL ENDOCRINOLOGY

Dr. Friedman: What part in terms of the groups of things you did--I mean aside from liking to do the research and laboratory work and so forth--of the fields of endocrinology, which parts did you enjoy the most or get the most out of, do you think?

Dr. Kaplan: I think probably, as I said, the fetal endocrinology. That I really enjoy the most. I really had enjoyed that. That was very stimulating. It was somewhat different, and I think we continue to do this--even after Dr. Gluckman left although he was very important for carrying out a lot of the studies that we did. But that was a major interest of mine--aside from the other things that I did. I would say that was first on line. I enjoyed the clinical studies, too, but I really enjoyed the fetal endocrinology studies.

SERVICE TO THE ENDOCRINE SOCIETY

Dr. Friedman: What part of your work for the Endocrine Society has felt most gratifying?

Dr. Kaplan: I think the council. There were a lot of things that we were involved in at the time that were very important. As I recall Ganong--and several others who were presidents for the three years that I was on--and there were a number of things that we tried to institute and get changed. You know, I think that's a group that has a lot of power to make changes in the Endocrine Society--running--and to have some impact, to some extent anyway, depending on whether the others agree with you. I don't know whether I should be pleased with having been on the group that selected the emblem--or whatever we called it--for the Endocrine Society. I was on the committee when we had to choose that, so that was part of my--if you consider that a high accomplishment--but that was one of the things we had to do. But the interaction with all the others, I think that was to me my best part of the time that I was on any of the committees that I was on. I enjoyed the council the most.

Dr. Friedman: How did you happen to get in the Lawson Wilkins Society? I was under the impression that was only related to the people who have been his former fellows and associates

[and] just because they're all known pediatricians?

Dr. Kaplan: No. Actually, they were some of the ones who were the organizers, but I was part of it because I have been in endocrinology for a long time--when they organized the Lawson Wilkins Association--but it includes now all the pediatric endocrinologists.

Dr. Friedman: I didn't know that.

Dr. Kaplan: Yes. It's a pediatric endocrine--it's in honor of him they call it the Lawson Wilkins Pediatric Endocrine Society, but it really is a society for pediatric endocrinologists. So it includes by and large all the pediatric endocrinologists in the US, and there are ones who have an honorary membership from various countries in Europe and South America.

Dr. Friedman: Is there anything you think I should know about yourself, which would enhance this biography--which is in essence what I've gotten today--that I didn't ask you about?

ON BEING RECOGNIZED FOR BOTH COLLABORATIVE AND INDEPENDENT ABILITIES

Dr. Kaplan: No. I think that I'm not as outspoken at meetings as I might be. I am more outspoken at small gatherings, and I think that a lot of what I've done is in collaboration with Dr. Grumbach. So perhaps I don't feel that I always get credit for what I may have done on my own. But I have to say that I have always felt more for the Endocrine Society than for actually the Pediatric Society--not the Lawson Wilkins--but the general Pediatric Society. I have received more independent recognition from them than I have from pediatrics, and I am always very grateful to the fact because I feel that members of the Endocrine Society have recognized my independent abilities more than some have.

Dr. Friedman: Because your work is endocrinology.

Dr. Kaplan: I know, but I am saying that, you know, they've appointed me to committees, which are independent of what I've done with Dr. Grumbach. Whereas, I haven't been appointed to any committees in the Pediatric Society. I don't mean the Endocrine Pediatric Society. So--

Dr. Friedman: I understand.

Dr. Kaplan: I've been grateful for that. It's always difficult when you're in a collaborative relationship to be able to have people identify what may be your independent abilities and recognize what required your abilities, solely. That's fine. I mean I've had a long time in endocrinology. I've enjoyed what I've done. I'm grateful for everything that people have recognized that I've done.

Dr. Friedman: You've had a wonderful career.

Dr. Kaplan: I'm still doing. I'm still organizing research activities and just put in a grant to

Genentech, which has been awarded for doing some studies.

Dr. Friedman: You _____?

Dr. Kaplan: Yes.

Dr. Friedman: I had dinner Saturday night with Barry Sherman.

Dr. Kaplan: Oh, yes.

Dr. Friedman: What brought me here was a _____ and Barry Sherman was seated at the same table I was. He wanted to know what I'm doing here.

NATIONAL COOPERATIVE GROWTH STUDY

Discovering that contaminated growth hormone was given to patients

Dr. Kaplan: [laughter] Yes. I know Barry Sherman. I have many contacts with him. I was the principal investigator for the National Study of Genentech Growth Hormone [National Cooperative Growth Study] the first time that they tested their biosynthetic preparation; I was the principal investigator in charge of that investigation. That was satisfying in terms of the work trying out that--you know [pause] I think the most devastating thing that occurred was to find out that some of the growth hormone we were using had caused Jakob-Creutzfeldt disease, and that was really a story into itself. That was very devastating. As to have to come to the determination that we had to stop growth hormone in all these patients and had to tell the families that there may be a chance that the patients got infected with a disease for which we had no cure, for which we had no test--until the time that they develop symptoms--which we could do anything about. That was a very difficult time.

Dr. Friedman: When was that?

Dr. Kaplan: We've had only one patient of the ones we've treated who developed it, but one here and two or three in New York. But that was after we left that they developed it. So that was a very difficult time--for all the time was spent in working with growth hormone.

Dr. Friedman: Well, thank you very much, Dr. Kaplan. It has been a very informative morning.

Dr. Kaplan: [laughter] Okay. I hope so. It's hard to know exactly what, you know, to give all the information in this way, but I have enjoyed talking about it.

Dr. Friedman: Thank you.

End of Interview

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