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J. LESTER GABRILOVE, MD

Interview conducted by
Adolph Friedman, MD
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EARLY EDUCATION

Dr. Friedman: We were talking about some of your growth, background, and so forth, and I was wondering, how come you were three years ahead of me, when we were born in the same year? Did you get through school very rapidly?

Dr. Gabilove: Well, in grammar school, I skipped four times, so I finished before I was twelve years of age. Then I went to a special high school, Townsend Harris High School, which was a three-year school. I got out of there within the next the three years, so those are the three years. When I went to college, I would have been finished earlier, but I didn't take one of the required courses until the fourth year, so they kept me in school.

MOUNT SINAI HOSPITAL

Dr. Friedman: I see. We talked about the history of Mount Sinai Hospital and the Department of Medicine at your Endocrine dinner. Is there anything specific you can recall about that?

Dr. Gabilove: You mean when I came to Mount Sinai, or my internship and residency?

Dr. Friedman: Well, let's get through all of that. When you first got to Mount Sinai--getting to the point where they celebrated your retirement--is there anything about the history of medicine at Mount Sinai?

Internship and residency

Dr. Gabilove: Well, I came to Mount Sinai in 1940, and we had an oral examination. There were a lot of people being interviewed, and twelve of us were chosen after the examination, and I believe I was number three. At that time, there was a rotating

internship of about two years. [Danny] Burdick was number two. Burdick and I elected to take the extra year of pathology and bacteriology, so we started the first year in pathology and bacteriology. Then we had our rotating internship; and by the time we completed the rotating internship, it was the time of the introduction of residencies. I was appointed resident in medicine and stayed there as resident of medicine.

DAZIAN FELLOWSHIP TO WORK ON WATER METABOLISM WITH JOHN PETERS AT YALE

Dr. Emanuel Libman, who was the head of the Dazian Foundation, offered me a fellowship to wherever I wanted to go. At that time I was interested in water metabolism, so I thought it would be nice to work with one of the “giants” of water metabolism, Dr. John P. Peters, who was professor of medicine at Yale. I went to be interviewed by Dr. Peters, and he took me on. I was being paid by the Dazian Foundation, and I spent a year at Yale as a “fellow.” In those days there weren’t any fellowships, really, to speak of around. In that year I worked in the laboratory as well as on the wards with Dr. Peters; then I returned to Mount Sinai. I had previously applied to Johns Hopkins and had gone down to see Dr. Warfield Longcope. He said he’d be happy to offer me a job, but he had promised the last one to Robert Austrian, where his father was the chief of medicine at Sinai Hospital and professor of medicine at Johns Hopkins, so he didn’t have a vacancy for me. Later, when I finished at Yale, he offered me another position, but I couldn’t accept it because I had accepted something else.

RETURN TO MOUNT SINAI HOSPITAL

On becoming a liaison between endocrinology and diabetes mellitus

Dr. Friedman: The rest of that we have documented. Was there anything about the history of endocrinology at Mount Sinai that would be of documentary importance?

Dr. Gabrilove: There was no endocrinology department or division at Mount Sinai at that time. There were people who were interested in the thyroid; and, in fact, Dr. B. S. Oppenheimer and Sol Silver had published a paper on Cushing's syndrome a couple of years previously. Dr. Silver was interested in thyroid physiology, and Dr. Louis Soffer was there. He had come from Hopkins where he had been working in [George] Harrop's laboratory. When I came back to Mount Sinai, I went to see Dr. [George] Baehr, who was the chief of medicine, and he assigned me to be the liaison between what was supposed to be endocrinology and diabetes mellitus. At that time, Dr. Herbert Pollack was the head of diabetes. There was no endocrine division. Nonetheless, I was assigned to be liaison. So I worked in both diabetes and in the laboratory working with Dr. Louis Soffer.

Working with Dr. Louis Soffer on thiouracil in treatment of thyrotoxicosis; confirming the work of Ted Astwood; working in the Diabetes Clinic

I met Dr. Soffer when I was a resident, and I had written a paper on thiouracil with Morley Kent, who was the other resident. Then, when we wrote this paper, Dr. Baehr said we couldn't publish it without some senior author. So he assigned Louie Soffer to be the senior author. We published this paper, "The Use of Thiouracil in the Treatment of Thyrotoxicosis," and it was one of [the] early confirmatory papers confirming the work of Ted Astwood. One of the other confirmatory papers was by Bob Williams, who

subsequently became the chairman of the Department of Medicine in the newly established medical school at the University of Washington. I worked in the Diabetes Clinic; Herbert Pollack decided to move, and Henry Dolger was appointed in his place.

STARTING THE DIVISION OF ENDOCRINOLOGY AT MOUNT SINAI

Then we started an endocrine clinic in the late 1940s. We had a new chief of medicine, Alexander Gutman, who came from Columbia University. Since most of the university hospitals had divisions in the Department of Medicine, Gutman organized the department into various divisions and organized the Division of Endocrinology with Soffer and me. We had a clinic, in which Arthur Sohval joined us. Arthur became quite interested in the testis and the ovary. We also had Joseph Gaines, who was an obstetrician interested in the endocrinology of the ovary. We started the endocrine division with a laboratory, a clinic, and whatever else was necessary.

CONSULTING IN BRAZIL, IRAN, AND PERU

Dr. Friedman: Okay, thank you. Now I'd like to ask you questions about your experiences as a "visiting professor." I noticed in the CV that you had quite a few experiences as "visiting professor," and maybe we could talk about them, one at a time.

Dr. Gabrilove: Yes. Well, I was invited to Brazil, and I was a visiting professor at the University of Sao Paulo. However, the visit was occasioned by the governor of Sao Paulo, who wanted an endocrine consultation. They invited me to be visiting professor at Sao Paulo, and I also saw the governor in consultation. I met several people that I know, including [B. L.] Wajchenberg, who ultimately became chief of endocrinology at the University of Sao Paulo Medical School. Another time, I was invited to the University of

Teheran in Iran, and I spent time in Teheran--in Iran--Meshed, Iefehan, and Shiraz--speaking and teaching--and I think those were the two longest ones. I was also invited as a visiting professor in Peru in conjunction with a course I gave in endocrinology at the university.

Dr. Friedman: University of Peru?

Dr. Gabrilove: No. The University of San Marcos, which is one the oldest universities in the Western Hemisphere. I also spoke at the Cayetano Heredia, which was a new medical school. I also gave a short graduate course for about a week in Lima.

LEARNING GAS CHROMATOGRAPHY

Dr. Friedman: Was it between the two, or was the second one in Cayetano Heredia?

Dr. Gabrilove: Mostly at San Marcos.

Dr. Friedman: Okay!

Dr. Gabrilove: As the result of my going down there, a number of people came as “fellows.” Louis Sobrevilla later had a career with the Population Council; but because of the political situation in Peru, he ultimately left Peru. Dr. Roger Guerra spent a year with me, and I sent him up to Herbert Wotiz to learn gas chromatography, which I had myself learned the year previously at Wotiz’s laboratory, and he was able to carry out a gas chromatographic assay for testosterone. He subsequently went back to Peru, as did Sobrevilla, and he became dean of the Medical School and chancellor of the University; later he became a congressman. I think now he expects to be vice president of Peru.

Then another Peruvian came, Faust Garmendia, who became professor of medicine at the University of San Marcos. So it was a very productive visit to Peru.

OSTEOPATHIC MEDICINE

Dr. Friedman: I also noticed in the CV that you were a visiting professor to the New York College of Osteopathic Medicine, and that lasted ten years. Tell me a little about that.

Dr. Gabilove: Yes. One of my fellows, Ken Frieberg, was an osteopathic physician, and he became a member of the faculty at the Osteopathic College, and he invited me to give the course in endocrinology. So over a number of years, I went out there as a “visiting professor” to give part of a course in endocrinology.

Dr. Friedman: I assume that you’ve written several articles in Spanish and that your fluency in Spanish stems from these trips to Brazil.

Dr. Gabilove: Well, I was not fluent in Spanish at all, but I taught myself Spanish with a book and with a disk. And when I went to South America, I was able to speak and converse in Spanish; I gave the lectures mostly in English. Nonetheless, I remember some physicians speaking to me in Spanish, and either Roger Guerra or Louis Sobrevilla said, “Don’t worry, Gabilove understands you.”

DIAMOX AND THYROID FUNCTION; DIAMOX AS A MEANS TO LIMIT IODINE UPTAKE

Dr. Friedman: You wrote a couple of articles on Diamox and thyroid function. Would you mind giving me a little information on that?

Dr. Gabrilove: Yes. I don't remember now exactly how I came to it. Oh! I know how it was. Iodide is picked up and secreted, not only by the thyroid, but is also secreted in the saliva and in the stomach. I knew that--with that--Diamox was utilized--hyperacidity in the stomach--to treat. I figured that with Diamox we should be able to block the uptake of iodide in the thyroid, but it was very difficult to actually do because we were not interfering with organification of iodide. With one of my fellows, we gave Diamox to normal subjects and to the patients with hyperthyroidism, and we found that the uptake of iodine was markedly decreased. Recently, with the finding of the iodide supporter, I spoke to several people who had cloned it and asked them whether the Diamox interfered with it, but they said they didn't know. I hoped that one day that would tell us, because I'm confident at least that it may interfere with the normal physiological uptake of iodine, not the organification, but the preliminary inorganic iodide uptake.

Dr. Friedman: What was the ultimate result? In other words, if you took a normal person and did an iodine uptake with or without Diamox, what would be the result?

Dr. Gabrilove: You decrease the uptake with Diamox.

Dr. Friedman: I assume that's giving adequate time between the two tests.

Dr. Gabrilove: Oh, yes! Yes!

CUSHING'S SYNDROME AND CARCINOIDS OF THE PANCREAS

Dr. Friedman: Again, I'm going to change the subject, but there was a paper in your bibliography entitled "Cushing's Syndrome and Avascular Necrosis of the Bone

associated with a Carcinoid-islet Cell tumor of the Pancreas.” Would you give me a run down on that paper?

Dr. Gabrilove: Well, we saw a patient with Cushing’s syndrome; and after some investigation, we decided the basic lesion was in the pancreas. As I recall, she had a carcinoid; and I don’t think we extirpated it completely, but she developed aseptic necrosis. As you know, Cushing’s syndrome can be associated with carcinoids of the pancreas. We reviewed the literature on it and told of our experience.

EARLY WORK ON THE FEMINIZING ADRENAL TUMORS AND THEIR EFFECTS ON THE TESTIS

Dr. Friedman: There was another paper on “The Effect of Feminizing Adrenal Tumor on the Testis”.

Dr. Gabrilove: Yes.

Dr. Friedman: Now you also wrote on changes in the testis in Cushing’s and other non-testicular disorders, and also in interstitial cell tumors of the testis, and Sertoli cell tumor of the testis. Is that too much for one question?

Dr. Gabrilove: I think that’s a little too much for one question, but I can start in by telling you that I was interested, of course, in Cushing’s and adrenal cortical disease and adrenal cortical tumors. A cardiologist referred a man to me who had edema. Well, to make a long story short, I decided that he had an adrenal cortical tumor and that it was a feminizing tumor. We studied this man very intensively. We described practically everything to be known about feminizing adrenal tumors, including the effects on the testis and about the elevation of estradiol. I then wrote a review of feminizing adrenal

tumors in *Medicine*. In fact, later, one of my friends from Montreal came across a feminizing tumor, and he looked up the literature. He was going to write a paper on the subject, and he told me, "You covered everything. There was nothing for me to write." One of the important lessons I learned was that patients with feminizing tumors have marked changes in their testis with hyalinization and fibrosis.

Dr. Friedman: But the tumor is not of the testis.

Dr. Gabilove: No! The tumor is in the adrenal, but the excessive estrogen results in hyalinization and fibrosis of the testis. But what was even more surprising to me was that after you remove the tumor--and they're at least better for a while until they get a recurrence--the testis histology markedly improves and the fibrosis and hyalinization are not as permanent as one would be led to believe.

Dr. Friedman: Does the testis then produce more testosterone?

Dr. Gabilove: Yes, and even spermatogenesis. At a later date in Cushing's syndrome--I don't know what led me to it--I started to study what happened in the testis. I imagine because it was of my experience with feminizing adrenal tumors. I found that in male patients with Cushing's syndrome there was a marked decrease in testosterone. This has since been confirmed in many instances.

Dr. Friedman: We were talking about changes in the testis in Cushing's. What about changes of the testis in other endocrine disorders, like thyroid disease and other non-testicular disorders?

Dr. Gabrilove: Robert Browning once wrote when asked about the meaning of a poem that he had written, “When I wrote it, only God and Robert Browning knew, but at the present time only God knows.”

GYNECOMASTIA AND OTHER FEMINIZING SYNDROMES

Interstitial cell tumors of the testis; Sertoli cell tumors

Dr. Friedman: Here’s an article on the testis and Cushing’s syndrome.

Dr. Gabrilove: Yes, I think I told you about the testis and Cushing’s syndromes. I also wrote about the interstitial cell tumors of the testis.

Dr. Friedman: Let’s talk about that.

Dr. Gabrilove: Because of my interest in feminizing syndromes, we, of course, described the abnormality in the testosterone-estradiol ratio in gynecomastia and the pathogenesis of gynecomastia. We were also interested in other feminizing syndromes, such as the feminizing interstitial cell tumor--where the tumor results in marked feminization--as do Sertoli cell tumors, which also result in feminization.

Dr. Friedman: What particular affect do the feminizing adrenal tumors have on the testis? Is it just the hyalinization and fibrosis, or are there other changes?

Dr. Gabrilove: Those are the essential changes. They get impotence; and I don’t recall that we measured the testosterone in that patient, but I think that it would be markedly decreased.

THYROTROPHIN'S ROLE IN ADRENAL CORTICAL DISEASE**Treating hyperpituitarism and adrenal cortical hypofunction with TSH**

Dr. Friedman: We had gotten to the point where we were going to talk about the effect of thyrotrophin on the testis.

Dr. Gabrilove: Well, I don't think we studied the affect of thyrotrophin on the testis, but we did study the affects of thyrotrophin in adrenal cortical disease. I was interested in whether patients with hyperthyroidism were compromised in regards to their adrenal cortical function, so I took a patient with hyperpituitarism and secondary adrenal cortical hypofunction and treated him with TSH. I must admit that this would not pass the institutional research administration at the present time. I gave him TSH, and with TSH we threw him into atrial fibrillation and adrenal cortical insufficiency. We stopped the TSH and his adrenal insufficiency improved and the atrial fibrillation returned to normal. But as I recall, we measured the adrenal cortical steroids, and they disappeared from the urine.

Dr. Friedman: That was good suppressive effect from the hyperthyroidism.

Dr. Gabrilove: Yes.

Dr. Friedman: Well, it's known that hyperthyroidism in a borderline adrenal insufficiency can throw patients into failure. It's a parallel to that.

Dr. Gabrilove: But it wasn't known, then.

ADRENAL CHANGES IN PREGNANCY**Post-bilateral adrenalectomy in pregnancy; early work on adrenal cortical insufficiency**

Dr. Friedman: There was another subject, which was mentioned in your bibliography, “adrenal changes in pregnancy.” Another question related to that is how about post-bilateral adrenalectomy in pregnancy.

Dr. Gabrilove: Well, you must recall the history and knowledge of the adrenal cortex markedly improved over the recent years. In the time when we studied this, we knew very little and didn’t know what was going to occur--whether it was safe for a patient with adrenal cortical insufficiency to become pregnant. So we encountered such a patient, and we studied what her adrenal function was and what happened during pregnancy. One of our studies was on thyrotoxicosis in a patient with Addison’s disease. There, too, we knew very little in the past, and we were interested to see what occurred during pregnancy.

Dr. Friedman: What did you find? Do you recall?

Dr. Gabrilove: I don’t recall now. I’d have to look at the paper to tell you. As I told you about Robert Browning--

RECENT WORK: PROSTATE GLAND AND ANDROGENS

Dr. Friedman: You also wrote later the “Effect of Long-acting Gonadotropin-releasing Hormone Analog (leuprolide) Therapy on Prostatic Size and Symptoms in 15 men with Benign Prostatic Hypertrophy.”

Dr. Gabrilove: Well, this was one of my favorite topics in recent years. I decided that--since the prostate was androgen dependent--that if we got rid of the androgens, we ought to be able to shrink it. It's true that some people had been treating prostatic carcinoma with androgen removal, but nobody had studied benign prostatic hypertrophy. Although there were reports of Koptics (a religious sect in Russia who practiced ritual castration), who--subsequent to castration--their prostates presumably shrank. So I decided maybe this is a very good way to treat benign prostatic hypertrophy. We got a grant from Abbott-Takeda, and we studied a group of patients. It does have remarkable effects on shrinking the prostate, but it causes a decrease in libido and sweating. The decrease in libido and potency was what made the Abbott people unwilling to continue support for this, although it shrank the prostate far more than treatment with Proscar. We had patients who had catheters in and, subsequently, could have their catheters removed. The prostate shrank perhaps forty to fifty percent, and they did very well. In fact, if you have someone who is unable to be operated on and has acute urinary retention, it's worth giving luteinizing hormone-releasing hormone. You can get them to overcome their obstruction and carry them along.

GYNECOMASTIA; KLINEFELTER'S SYNDROME

Dr. Friedman: After these recent questions--which re-stimulated your thoughts on some of your past work--is there anything you think I should know that I did not ask you about--that you would like to tell me?

Dr. Gabrilove: Well, you know what my favorite topics were. One was gynecomastia. I don't think I spoke on gynecomastia.

Dr. Friedman: Go ahead.

Dr. Gabilove: Gynecomastia is the enlargement of the male breast. While I was studying feminizing adrenal cortical tumors, it occurred to me that patients with feminizing adrenal cortical tumors get enlargement of the breasts. I was also studying Klinefelter's syndrome. Now with Klinefelter's syndrome, I reasoned that the patients who had a karyotype of XXY should produce less testosterone and more estrogen than the normal male because they had an extra X ordinarily. In the male, there is more androgen and less estrogen than in the female, who has more estrogen and less testosterone--because of the XX in the female and the XY in the male. So we measured the testosterone and estradiol, and--sure enough--testosterone is decreased and the estrogens increased in the patient with Klinefelter's syndrome. In fact, if you take a group of men of all different ages with Klinefelter's syndrome, you will see a decline of testosterone over the years and a rise in estrogen, which sort of parallels what is seen in the normal person who ages. We wrote a paper in which we said that: in Klinefelter's syndrome, a testis--which appears to be functionally already aged--continues to age. It's surprising that people write on Klinefelter's syndrome, but nobody ever mentions what the biosynthetic defect is. It's already there for them to read, but apparently they don't believe it--or they haven't read about it. So I was very interested--because they had gynecomastia, and because we had patients with feminizing tumors who had gynecomastia--what was the mechanism of gynecomastia? We then took out the slides of patients who had been treated for prostate carcinoma with stilbesterol and estrogen. We found the following: as far as gynecomastia was concerned, early in gynecomastia you get hypertrophy of the ducts with a very succulent connective tissue, and then--after a

period of two years--you get fibrosis and sclerosis around these ducts. So I thought this explained why some children who get gynecomastia in puberty get the persistent gynecomastia. Most children with pubertal gynecomastia--for whatever reason--readjust and put out the right amount of androgen and estrogen. Much later, we had a man who came complaining of losing his hair. He had gone to a dermatologist, and the dermatologist gave him some cream and said, "Here, this will help you." Sure enough it did, but he developed gynecomastia and impotence. It was apparent to me that he must have estrogen in the cream. We measured his semen estradiol, and it was very high. We stopped the estradiol and asked him whether he wanted to continue with the cream, or not--because if he continued the cream, he'd have loss of libido, potency, and would continue to have enlargement of the breasts. He thought about it for a while and decided he would rather lose his hair. We stopped it, but his gynecomastia never subsided because he had been on estrogen for several years. This was what I thought was the mechanism for those children who have persistent pubertal gynecomastia--relatively uncommon because, in most children with gynecomastia, it disappears.

Dr. Friedman: It fades away after puberty.

Dr. Gabilove: There are some children with gynecomastia who won't go to school, won't go swimming, and some have to have surgery. I said that this is the mechanism--that whatever is going on--as far as estrogen is concerned: if it lasted more than two years, then gynecomastia persisted. So we've had a lot of experience with feminizing syndromes, and we became much interested in--and as I told you, we studied the feminizing adrenal cortical tumors, the Sertoli cell tumors, [and] feminizing interstitial

cell tumors in association with gynecomastia. So this was one group of studies that we were interested in. We were also interested in Cushing's syndrome, and we had a whole host of papers on Cushing's syndrome.

CUSHING'S SYNDROME AS A PEDAGOGIC TOOL

Dr. Friedman: That was Soffer's influence, wasn't it?

Dr. Gabilove: Well, he started it, but Angelo Iannaccone came as a visiting fellow and wrote up most of these things. Most of the patients were studied by me. I was the gopher, the doer. Soffer sat in the office. I was the doer, and Angelo worked with me. And then we gave Angelo the writing up, so he could go back to Italy where he became professor on the basis of these articles. So because of Cushing's syndrome, I became interested in other adrenal disorders. I described virilizing adrenocortical adenomas, which are very interesting, in addition to the feminizing adrenocortical adenomas. Virilizing adrenocortical adenomas are very often benign, even though they're very large. In incidentalomas, people utilize their size to decide whether the tumor is a carcinoma or not--based largely, in fact, on non-functioning tumors and the tumors in Cushing's syndrome. But everyone forgets that virilizing tumors can be very large and entirely benign. On the other hand, in the feminizing tumors--no matter how they look--if they are more than 200 grams, they're malignant.

Dr. Friedman: That's good to know.

Dr. Gabilove: There are some interesting stories about it, but I won't bore you with it at the moment. Cushing's syndrome, feminization and gynecomastia, adrenal cortical

tumors, and the benign prostatic hypertrophy have been the greatest interest to me, as well as the early studies on the thyroid.

CURRENT RESEARCH: POLYCYSTIC OVARIES

Dr. Friedman: What are you doing now--anything?

Dr. Gabrilove: Yes. I'm still working. I run the fellowship program, and we're now starting some other studies on polycystic ovaries.

Dr. Friedman: Do you have any ideas on why the polycystic ovaries get insulin resistant?

Dr. Gabrilove: I have a number of ideas on that, but I'm not at liberty to discuss it at the moment because it may turn out to be very important.

JOYS OF TEACHING AND TRAINING OVER ONE HUNDRED FELLOWS

Dr. Friedman: Okay, sir. Thank you very much for this additional time, and I will eventually get this back to you. About the fellows you trained--how many and who they were.

Dr. Gabrilove: Well, I've trained over one hundred fellows, and that's been a great delight. I told you before that one of my fellows may be vice president of Peru and was chancellor of the University of San Marcos. Among the fellows I trained was Alice Levine, who worked with me on the prostate, Angelo Iannaccone who worked with us on the Cushing's, and Jack Gallen, who is also very interested now in the prostate. In those days, we were just studying adrenal cortical function. A number of our fellows are now on our faculty at Mount Sinai, and others are in academic life elsewhere. _____.

Alex Stagnaro-Green is dean of student affairs. I told you that my Peruvian friends were professors of medicine in Peru. Many of the fellows have gone out into practice. One of my former fellows, Paul Jellinger, is president of ACE [American College of Endocrinology], and another former fellow, Rhoda Cobin, is the president-elect of ACE. And Donald Bergman, a third former fellow, is the secretary treasurer and, I imagine, ultimately will be president. Many of the former fellows are chiefs of endocrinology at other hospitals. Walter Futterweit is the expert on the polycystic ovary syndrome .

Dr. Friedman: I'm surprised that [David?] Baskin let these jobs go to new people.

Dr. Gabilove: Well, they're very good.

Dr. Friedman: Okay. Thanks again.

End of interview

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