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LESLIE J. DEGROOT, MD

Interview conducted by
Michael Chappelle
June 10, 2009

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INTRODUCTION

Leslie J. DeGroot, MD, Research Professor, Department of Cellular and Molecular Biology, University of Rhode Island, is an internationally recognized endocrinologist and an expert in thyroid physiology. He has made important research contributions to a wide spectrum of topics in the field, including the understanding of thyroid synthesis and its mechanism of action, iodine metabolism, thyroid cancer, and autoimmune thyroid disease. As a pioneer in these areas of clinical investigation, Dr. DeGroot is widely regarded as one of the founders of modern thyroidology.

BIOGRAPHICAL SKETCH

Leslie DeGroot was born in 1928 in Fort Edward, New York. He attended Union College and received his medical degree from Columbia College of Physicians and Surgeons in 1952. Following an internship and residency at the Columbia Presbyterian Hospital in New York City, Dr. DeGroot worked at the National Cancer Institute in the endocrinology branch with Monte Greer in 1955. After spending the first half of 1956 in Afghanistan as a medical missionary and public health physician, he returned to the United States to do an endocrinology fellowship with John Stanbury at Massachusetts General Hospital (MGH). Upon completion of his medical training in 1957, he continued collaborating with Dr. Stanbury at MGH for a total of eight years. During that period, he also began teaching at Harvard Medical School. When John Stanbury relocated his laboratory to the Massachusetts Institute of Technology in 1966, Dr. DeGroot moved there as well, and they continued their collaboration. Two years later, Dr. DeGroot was recruited by the University of Chicago to become professor of medicine and director of the Thyroid Study Unit. In 2004, Dr. DeGroot retired from the University of Chicago and accepted the position of professor of medicine at Brown University. In 2008, he relocated his laboratory to the University of Rhode Island, where he is currently research professor in the Department of Cellular and Molecular Biology.

Dr. DeGroot was president of the American Thyroid Association and has been recognized with numerous awards and honors, including the Distinguished Service Award from the American Thyroid Association and the Distinguished Educator Award from the Endocrine Society. He has authored more than 450 original research papers and has contributed to the field as a developer and editor of two authoritative textbooks: *The Thyroid and Its Diseases* and the encyclopedic *Endocrinology*. Recognizing the usefulness of the World Wide Web as an important source of medical information, Dr. DeGroot converted *The Thyroid and Its Diseases* into a Web-based textbook, "ThyroidManager" and subsequently developed a comprehensive Web-based source Endocrinology, "Endotext," <www.endotext.org> written by 400 authors. These Web-books provide a current, complete, downloadable, and free source of information to physicians, researchers, and patients around the world.

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I. FAMILY BACKGROUND AND EARLY YEARS

Chappelle: Dr. DeGroot, please tell me a little bit about your family background, beginning with your grandparents.

DeGroot: My grandparents--there being four--one set was born in Holland. Both immigrated to this country around 1870 or 1880 to upstate New York, actually to a farm in upstate New York, north of Albany. I don't happen to know their educational background. Then the other side was Scotch and English immigrants who had come much earlier, but I don't know just how long ago, and lived in upstate New York. My Dutch grandparents ended up on a farm, which became our farm, and my other half of grandparents settled in a little town called Fort Miller, which is not far from where our farm is.

Chappelle: Were your parents farmers?

DeGroot: Oh, yes. My grandfather and grandmother, on my father's side, Henry De Groot, was a farmer and had a dairy farm of about one hundred and twenty acres or so, and they sold milk, locally, and whatever they could sell. He had four children, including three sons--including my father. My father stayed on the farm and actually bought the farm next door and ended up with two farms--a couple of hundred acres--and he was the farmer, and then I grew up on that farm.

Chappelle: What type of education did you have?

DeGroot: I went to a country school that had twelve students for a while, then a local school in town, and then a high school in Fort Edward, New York, then Union College in Schenectady, and then Columbia Medical School.

Chappelle: When you were growing up, did you have any activities, sports, or hobbies that you particularly liked?

DeGroot: Well, I helped on the farm--a *lot*. I mean it was normal to help on the farm. And I helped on the farm. And I liked to hunt and trap, and I ran trap lines, and I did a lot of hunting and walking through the woods, never much killing, but a lot of shooting. In high school, of course, we played sports. We skated and played softball. In high school I also played in the high school band and orchestra, but I didn't play any sports in high school. There were other things, but those were the main activities.

Chappelle: Were you making any decisions in high school about what you might want to be doing later in life?

DeGroot: It was assumed without discussion that I was going to go on to college, and without a definite plan, but it was always clear that I should head to college. And I really intended to be a chemical engineer--or I guess chemical engineer, but chemical something--when I went to college. That was my goal. I think I do know why. I had a high school teacher--his name was Jack Leonard--who was a very personable guy and did experiments that were interesting, and it got me interested in chemistry. I think that probably is why.

II. UNION COLLEGE (1944-1948)

Chappelle: Why did you choose Union College?

DeGroot: Well, I didn't know much about colleges. I mean, I'd never heard of Harvard, let alone others. And it was nearby, and it was considered a very good school, and they gave me a good scholarship. So, several reasons.

Chappelle: And did you continue to work on the farm?

DeGroot: In the summer, yes. School was out in June and started sometime in September; in between, I certainly worked on the farm all summer. And I rarely, but sometimes, had to come home and actually run the farm for a week or two when my father was ill, but that was, fortunately, exceptional.

Chappelle: What was campus life like in college during the mid- to late-1940s?

DeGroot: I started in '44 and ended in '48, so this was right before and at the end of the Second World War, so the return of veterans was a dominant factor. So there were two distinct groups: the younger people and a bunch of guys who were veterans that had had a lot different life experience than we had had. But other than that I think it was pretty normal. I joined a fraternity; I had several jobs while I was there--I had to work part-time--and active in a variety of college extracurricular activities. We lived in a fraternity house and had a terrific time. I spent a lot of time drinking and chasing women and having a good time and also working.

Chappelle: What was your major?

DeGroot: Well, at first it was chemistry, but then Union had a nice program called a division 3 major, which meant you were in science, but it didn't specify an exact particular slot in science. And it allowed you to take courses in liberal arts, without having a major in liberal arts. So my central area was science, and then I took other courses in economics and similar courses.

Chappelle: Did you have any special contact with the faculty?

DeGroot: I mentioned economics because it was fortunate to be able to take upper-class courses without having to go through a set of pre-requisites to get that level. And I had a teacher whose name was John Lewis, who taught economics. He was a very gifted guy--actually became a member of the President's Economic Advisory Council under Eisenhower, I think. Then I had a couple of very good teachers in genetics and in embryology, although I blush to admit I can't remember their names. Anyway, they were courses that I found very interesting, and they were very good teachers. But the one person whose name sticks in my memory is John Lewis, John E. Lewis.

Chappelle: What decisions were you making regarding a career in medicine?

DeGroot: At that point--I don't think in college most students have any vague idea of what medicine is actually about--except it deals with sick people--at the practical level. I certainly had no idea what medicine was about, but I did know it had to do with caring for ill people, and that it was a science, in part. I was intending--after my second year, I was clearly intending to go to medical school.

III. COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS (1948-1952)

Chappelle: How did you choose a medical school?

DeGroot: Well, the same sort of not very logical approach. The medical schools that I really considered were Albany Medical College and Columbia. As I said, I really didn't even know about schools in Boston or other areas. And I really didn't apply to them. I applied to Columbia, and they offered me a scholarship--full scholarship. So that was quite an enticement. So I went to Columbia.

Chappelle: How were you supported as a student?

DeGroot: Well, my Pop gave me some money, and I had a job all the time I was there. I served meat on the cafeteria line; I was a technician doing blood counts and chemistries--and did a lot of that. But I had a job all the time, and with my Pop's support and full tuition, I was able to get by.

Chappelle: Did you still work on the farm, sometimes?

DeGroot: Well, after the first year, I couldn't. At the end of the first year, we had three months off, and I was home, then. But then after that, really, I was gone from the farm except on vacations for a few days.

Chappelle: Did any of the part-time jobs you had spark an interest in endocrinology?

DeGroot: No, I don't think so; they just gave me some food to eat. [laughs]

Chappelle: Who was your mentor?

DeGroot: Well, mentor is a little complicated. The guy who was the most dramatic force at P&S [Columbia University College of Physicians and Surgeons] was Robert Loeb, who was professor of medicine; he was a very austere guy, who I think was a terrible judge of human nature, actually, but who demanded very high-level performance. He really didn't accept anything except high-level best. And he was a very tough customer, and he was very hard on medical students--frequently would just tear them apart for very little reason. And people were in awe of him. And I think, in terms of thinking--not thinking--but ingraining my own attitude about work and how to do things, he was a mentor. But as a personal confidante and a person helping with a career, he wasn't. And actually I don't think that I had one at P&S. I had my roommates--you know, we'd talk--and other people. But I don't think that I really had a mentor other than Loeb, and he was only sort of a mentor.

Choosing endocrinology and thyroidology

Chappelle: What type of physician were you thinking of becoming?

DeGroot: Well, I liked internal medicine, so I sort of had an interest in internal medicine. Because of Robert Loeb's interest, I was interested in nutrition, not in the sense of a diet, but in the sense of metabolism in the body. He was very interested in that area, and that sort of rubbed off on me. And I was also interested a little bit in the thyroid and endocrinology because of a guy whose name was Sidney Werner, who was an interesting and bright and scrappy guy. I kind of enjoyed his personality.

Chappelle: And he was in the thyroid field?

DeGroot: He was in the thyroid field, yes.

Chappelle: When you started to look at the thyroid at that time, what attracted you to it?

DeGroot: I cannot say that my career was well thought out, as you can easily tell. At the end of my two years of residency, I was uncertain what I was going to do. I actually wanted to go to work with a guy whose name was Ted Van Itallie, at Saint Luke's, working on nutrition, but he didn't really have a spot and/or money to support me.

Clinical fellow at the National Cancer Institute, NIH (1955)

And I was looking around as to what to do, and I was drafted. I got a notice: You've been assigned to the draft and you're going to go in the Navy. Several people at P&S had gone to the NIH and had positions; and if you did that, it qualified as military service as the Public Health Service. So I drove down or, I don't know, took the train to Washington D.C. and went to the NIH and met the guy who was heading the endocrinology branch of the National Cancer Institute. I had learned that they had an opening. And I went there and was able to apply for and receive a position at the National Cancer Institute and then was able to get my way out of the Navy into the Public Health Service. And the person I was assigned to work with was Monte Greer, who was a thyroid researcher. So that's why I was telling that story.

Chappelle: So your interest came by way of the people that you knew who were interested in the thyroid, not necessarily because you were interested in that particular field.

DeGroot: Absolutely.

Chappelle: Then you grew to--

DeGroot: It was because I--well, there were several--but Monte Greer was my mentor at the National Cancer Institute, and we became very good friends, and he was a very, very fine guy, and certainly sparked my interest in research in that field. We published a paper together, and we competed for a prize together. There were several other young people in that same group, so there was a nice camaraderie and a nice intellectual stimulation. And then he became the conduit to go on to work with John Stanbury at MGH. He helped me get into that. So that's when I really got into the thyroid.

Marriage

Chappelle: You met your future wife, when you were still at Columbia?

DeGroot: Yes.

Chappelle: What was her background and career?

DeGroot: We met at opposite sides of the bed, caring for a young woman with--we both remember it very well--a young woman who had rheumatic heart disease and was in an oxygen tent. And we were rotating tourniquets on the limbs, which is what one did in those days for heart failure--one of the things. And she was a

very attractive young woman. And I became interested and fortunately was able to eventually convince her to marry me. She lived in New York--her father actually ran a mining company--quite a different background from mine. She was a student nurse at Columbia.

Chappelle: Did you have any children?

DeGroot: We had five.

Chappelle: Are any of them in medicine or science?

DeGroot: My daughter is in medicine--in AIDS and immunology research and vaccine research--now at the University of Rhode Island. She has her own biotech company that does this work and has NIH grants. My son is an orthopedic surgeon at Newton-Wellesley Hospital in Boston; his wife is an obstetrician. And another daughter's husband is an internist. So we have quite a few doctors [in the family].

IV. PRESBYTERIAN HOSPITAL (1952-1954)

Chappelle: How did you come to do your internship and residency at Presbyterian Hospital?

DeGroot: I guess, in part, because I was lucky to get there. At the time I was going into residency, the three best places in the country were Mass General [Massachusetts General Hospital (MGH)], P&S, and Hopkins. Hopkins was far away, and I actually was accepted at MGH and at Presbyterian. And I'm not exactly sure why I chose--I don't remember exactly. I mean, I'd lived there; I knew it, maybe that helped. But it was considered one of the very best programs, and I felt lucky to be there.

Chappelle: Was there any feature of your internship or residency that stands out?

DeGroot: Well, you know, it's a fantastic time in a young doctor's life. There are various things that happen. One is that, as a medical student, you're sort of treated like a king. Nothing bad happens to you, really. When you become an intern, you get on the bottom of the totem pole, again. [laughs] Totally. You suddenly switch roles and you're--especially in those days--you're the scut-boy. But the other thing, the thing that's more important or really important--that [being at the bottom of the totem pole] is just trivial--is the fantastic immersion into medicine. I mean, all of a sudden, one day you're a student, and the next day you're in charge of taking care of people. It's a fantastic immersion. Now it's not quite so heavy duty, but we didn't have a lot of time off. We might have a day or two off every other weekend, but we worked, certainly, twelve-hour days, five or six days a week, and had night call. I mean, it was heavy duty, big immersion, and a wonderful experience. You just are learning and growing so much in your career. I don't

know what other people felt, but I know that people I was associated with had that same sense. I mean, you really haven't got time to think about world issues and your future career too much; you're sort of totally involved in doing your job.

Chappelle: When you finished up with your residency, before the draft, how did you imagine your career was going to go?

DeGroot: Well, I was thinking of an academic career at that point although I didn't have a clear idea of what that would be or what that would amount to, nor the area. As I said, I had toyed with nutrition and possibly gastroenterology, and then ended up assigned to work with an endocrinologist. And so that's how carefully I thought it out. I'm sorry about that, but that's what happened.

Chappelle: Why sorry?

DeGroot: It would be nice if I could tell you that I had a carefully planned program from the beginning, but it wasn't the case.

V. THE NATIONAL CANCER INSTITUTE (1955)

Chappelle: When you got to the National Cancer Institute, you said you were working with Monte Greer.

DeGroot: Yes.

Chappelle: What was he working on when you started working with him?

DeGroot: He had a couple of interests. He was interested in neuroendocrinology, and actually he was quite advanced in what he was doing: mapping the hypothalamic nuclei by implanting electrodes in rats, then stimulating them and looking at responses and control of appetite and drinking behavior, and things like that. And he also was doing clinical work on the thyroid, evaluating the effect of certain drugs on thyroid physiology. He got me going to measure--actually he wanted me to measure thyroid-stimulating hormone in a biological assay in baby chicks using radioisotopes, and I set that up. And I worked with him in a study that had to do with sex hormones and thyroid function, but I've forgotten the exact nature. And then we were involved in a clinical study. We had patients in the clinical research center of NIH, and we were doing studies on the effect of drugs that were used in treating patients on the metabolism of thyroid hormones using radioactive iodide as a tracer element.

Chappelle: Had you decided on thyroidology at this point?

DeGroot: I'm not sure that I had, but I had spent a year in it, and had learned a lot about it, so now I knew that field better than any other. So maybe without making a clear decision, I was edging that way because of my training during that year.

United States Operational Mission to Afghanistan (1956)

Chappelle: Were you set on your career going towards endocrinology?

DeGroot: I think probably at that point, yes. But as you know, I got interrupted by a trip overseas for a year. What happened was [that] Monte Greer left, and I didn't really want to start off on a new program with somebody else for a year. And we'd always considered some sort of--going overseas and working as a medical missionary had been an idea. My family was quite religious, and I had that in the background of my head. And we were recently married, and we heard about an opportunity to go with the State Department to Nepal. And so we went looking for that, and eventually ended up in Afghanistan for a year.

VI. MASSACHUSETTS GENERAL HOSPITAL (1956-1968), HARVARD MEDICAL SCHOOL (1958-1966)

Clinical and research fellow (1956)

DeGroot: And then when I was in Afghanistan, I had to arrange to come back to finish my training, and I had by this time decided that Harvard was the place to go, and so I wrote and asked to come back to finish my residency at Harvard, and the chairman there arranged that I come back and spend six months working with John Stanbury in the thyroid lab, and *then* start my residency. So that kind of got me back into the thyroid research, and I think that's probably what cemented my program at that point.

Chappelle: But you weren't seeking to work with John Stanbury, and you weren't seeking to work necessarily on the thyroid? It [just] happened?

DeGroot: [laughs] It's an awful thought. But, actually, I did know who John was and did know that he was doing very high-class work, and that he had an outstanding laboratory. But I don't remember whether that was involved in my decision-making; it may have been. But Monte Greer wrote a letter for me, so that may have played into it as well.

John Stanbury

Chappelle: What was John Stanbury like as a scientist?

DeGroot: John was definitely a mentor. John was and is a very fine guy; I spoke to him yesterday. He's now ninety-five, maybe, and in good shape. He had at that time, really, the best lab in the world in that field, and it was oriented towards biochemical aspects of research on thyroid disease. He had a group of young people that came from all over, who were just terrific people. They all have gone on to very fine careers around the world: Italy, Belgium, France, England. I mean, they were very good people. And so it was a wonderful place to be. And John is a very nice Southern gentleman, kind of a Brahmin type. And also interested in proper--I mean doing research and doing medicine correctly--high standards. And he taught me a lot about that, and he gave me a lot of freedom. And he also taught me a little about writing; he used to go over my writing and correct it with a heavy red pencil [laughs] and taught me a lot.

State of the art thyroidology circa 1956

Chappelle: What was the state of the art in thyroidology at that time?

DeGroot: This started pre-anything. I mean, we did not know anything about DNA; we did not know anything about protein structure. We knew that genes must exist, but no gene had ever been identified. I mean, it's hard to imagine, in retrospect, how primitive our knowledge was at that time. This is 1956 [when] I started there. And things were *just* boiling up at that point. Basically, it was physiologic research on the effect of drugs or iodide deficiency or something on the thyroid, and it was biochemical research using the tools that had been developed to study intermediary metabolism in cells, in general. A lot was known: the Krebs cycle and this and that--a lot of biochemistry was already known--but nothing about genetics and molecular biology as it's known nowadays. So we worked on the metabolism of the thyroid cell; we worked on hereditary defects in thyroid hormone synthesis that caused thyroid hormone deficiency, and we worked on metabolism of radioactive iodide as a tracer for thyroid hormone.

Laboratory studies

Chappelle: What laboratory research did you do?

DeGroot: I did a lot of studies on iodide kinetics in humans: fed them radioactive iodide and measured distribution in thyroid, in blood, and urine, and feces, and tissues to some extent--analyzing the way the iodide was transported and incorporated into hormone and metabolized and excreted. Did that a lot. In the laboratory, I started working on thyroid hormone biosynthesis, and we purified an enzyme called thyroid peroxidase [TPO] that was involved in thyroid hormone. And we studied the energy supply--the source of the energy that created the hydrogen peroxide that was used in the biosynthesis of thyroid hormone. And we studied patients that had metabolic defects that made abnormal iodinated proteins, for example.

Advancing the field

Chappelle: How did this advance the field?

DeGroot: How did this advance the field? Well, the method of purification of the hormone--of the peroxidase--became the one that is generally used. It's not a Nobel Prize kind of thing, but it was the method that was used subsequently. The information on the generation of hydrogen peroxide was fairly unique. We found one source of congenital metabolic defect causing goiter; subsequently, there were five or six that were identified--there are many more now, but that was one of the ones that was being identified. None of them were world-shaking events; they were not Nobel laureate stuff, but they were good solid research studies and earned me some recognition in the first five or ten years of my career.

Colleagues

Chappelle: Who were your colleagues at this time?

DeGroot: The people in this lab, I mentioned, were outstanding people: A guy whose name is Aldo Pinchera, who eventually developed a wonderful program in Pisa, Italy; a young man whose name is Jacques Dumont, who became a very prolific and important thyroid researcher in Brussels; a guy whose name was Reginald Hall, who became an outstanding and widely respected thyroid researcher in England. There were a whole group of people from Austria, from Denmark, from Australia, all of whom were really wonderful researchers and people, and they were my intimate colleagues.

Laboratory tools

Chappelle: What tools were you using?

DeGroot: We used radioisotopes for many studies, especially the studies I was doing in humans. So we used scintillation counters to enumerate amounts of radioisotope. And we did chromatography, which is a way of separating radioactive iodide-labeled compounds in the thyroid, which is a very important technique. But then we used all kinds of other standard biochemical techniques, and I spent a lot of time working with an oxygen electrode, measuring formation of adenosine triphosphate during phosphorylation and energy consumption in mitochondria. And we separated proteins and analyzed them--and electrophoresis. We used standard biochemical techniques that were available at that time. And we used a lot of isotopes and a lot of chromatography.

Chappelle: Would you say that the lab work was technologically driven?

DeGroot: No. I think that always one has a question or a program, and you try to use the best technology you can find at the time. So it's technology limited, maybe, because you decide there's a question you're interested in, and then you figure out how you're going to approach that, and you use the best technology, but sometimes you can't do anything with the question at that moment. But I think it's technology heavy and technology limited when you can't do something, but I don't think it's driven by the technology.

On choosing lines of research

Chappelle: What factors determined what areas you were looking at? How did you choose from all your varied interests?

DeGroot: Well, the iodide kinetic work I really got into because John Stanbury wanted me to do it. He had pioneered studies in that field and endemic goiter. And he wanted me to continue it and employ it in studies on normal human physiology, which is what we did. Then the others were--some of the studies were determined by the fact that the patient came along that had a history of thyroid abnormality that hadn't been explained and had a big goiter, and we would study that patient and try to figure out why, what was wrong with the thyroid physiology. So that was a second way our research got directed, and it might be one kind of problem now, and in another six months we'd have a patient with another problem, and we would study that. So we pursued individual patients or families. And then the other area was more a trying to apply--at that particular moment--apply the knowledge of what was known in general about intermediary metabolism [in order] to understand how the thyroid processes worked in relation to making thyroid hormone, and control of making thyroid hormone. We adapted understanding [that was]--say learned in liver or some other tissue--and use those tools and techniques studying thyroid physiology.

Career opportunities at MGH

Chappelle: You ended up staying at the MGH for about nine years?

DeGroot: Twelve years, actually. Well, ten years there and two at MIT, but I was still at MGH.

Chappelle: And you would have been happy just to stay there?

DeGroot: Well, that's a complicated issue. I had been there twelve years. Or actually, I was there fulltime ten years, and then I was at MIT for two years, but my clinical practice and teaching was at MGH. I had never quite made it to be assistant professor, although I'd had promotions every year for ten years. But there are a lot of levels in between where I was and the next step. My fate probably was to find a job elsewhere, although at MGH at that time, you had to provide your own

support, and you did that by a grant and/or--usually “and”--practice. And I supported myself from research grants and practice, as did most of the people there. But probably my future would have been--had I stayed there--eventually to go to another medical center, someplace.

Teaching at Harvard; a normal day

Chappelle: And you became a member of the faculty of Harvard in that period, too. What kind of teaching were you doing at Harvard?

DeGroot: The teaching was clinical teaching. We taught second-year students history-taking and physical examinations, for example. And we taught third and fourth-year students on making rounds on patients, and doing consults, and in the clinic. It was all clinical teaching; it wasn't giving lectures.

Chappelle: How did you organize your day?

DeGroot: The normal thing was to go to the lab and work like hell. [laughs] I mean, do a lot of work. And we worked five days, and we often worked until six or later, and we usually--almost always--worked Saturday morning and part of Saturday afternoon. And then we'd typically spend one half a day seeing patients. And the rest of the time was in the lab. The teaching responsibilities were modest; they would be the equivalent of one half-day a week at the most.

Chappelle: A half-day a week?

DeGroot: At the most. If you're making consult rounds or doing a turn seeing patients as attending on the service, you'd be very busy for a month, but that would only be once a year or something. So I say, on the average the teaching responsibility was not more than one half-day a week.

VII. THE NEW ENGLAND JOURNAL OF MEDICINE (1961-1965)

Chappelle: Overlapping your last four years at MGH and Harvard, 1961-1965, you also were at the *New England Journal of Medicine*. How did that come about?

DeGroot: The editor, Joe Garland, had three associate editors, and one of them was a friend of mine, and he was leaving to go out to some place in California. And he suggested my name, and I was interviewed and just got the job, or the job got me--one or the other.

Chappelle: What were your responsibilities?

DeGroot: The responsibility was to read and review one third of all the journal articles submitted, which was at that time about ten to twenty a week--for each of the

three associate editors. And we reviewed them and wrote a little critique and gave it orally at the board meeting--the editorial board met every week with several very distinguished and austere Boston physicians. The editorial board was probably ten or twelve, and they were religiously there. It was considered a very important thing, and they also read some of the papers, usually one of them had read a paper. So they had an opinion, and then we gave a report. And sometimes they were farmed out to somebody outside, but that was not common. And then they were given some kind of score, and the editor decided to accept it or not.

Chappelle: How far had your career advanced at this point?

DeGroot: Well, I was a budding young researcher and investigator, still struggling upwards.

VIII. MASSACHUSETTS INSTITUTE OF TECHNOLOGY (1966-1968)

Chappelle: And how did you come to move to the Massachusetts Institute of Technology?

DeGroot: John Stanbury moved to MIT, and he asked me to go with him, basically, and offered a position as an associate professor, which sounded quite exciting. I think I was still paid out of my own research grant, but my pay probably went up a thousand or two, which was a lot in those days. And we went there to run a clinical research center, and basically I occupied my time doing research and running a clinical research center at MIT.

Chappelle: What clinical research did you do?

DeGroot: I did more studies on iodide kinetics with isotopes. And we continued our basic research on the metabolism of the thyroid and the formation of thyroid hormone.

Thyroid hormone resistance

But I met a young guy who came to see us, who had some strange cases that seemed like they might be due to resistance to the action of thyroid hormone, and I heard about them. And that was an idea that was not a unique idea at MGH because there had been--previously, under Fuller Albright--the recognition of resistance to parathyroid hormone. So there was in the MGH sort of the mystique of hormone resistance. So when I heard about these cases, that's what they sounded like. And so we started collaborating with this young guy--his name is Sam Refetoff--and we did a lot of work on that. These people lived in Watts, actually in Los Angeles. And we brought them out, and they lived on the clinical research center for a year: a boy and a girl and, eventually, the mother and another

child. And they also lived with us; they became part of our family at times. They were deaf mutes; that was one of the important points about them.

Chappelle: Who supported that research?

DeGroot: NIH.

Chappelle: Did that work at that time have any therapeutic implications?

DeGroot: Well, of course, we hoped so. But that became a very big field. And it involved the nuclear receptors and the study of the nuclear receptors. At that time we did not know that there were such things as thyroid hormone receptors. What we established was that these people had a metabolic rate and other signs that they were normal metabolically, even though their thyroid hormone level was twice normal. So they were clearly resistant to the action of thyroid hormone. Our studies evaluated the amount of hormone that was required by their body and the biochemical changes it produced, but mainly it found that they just didn't respond normally. Because they took twice as much thyroid hormone to turn on their metabolism as it did a normal person's.

IX. UNIVERSITY OF CHICAGO

Chappelle: Why did you leave MIT?

DeGroot: Some people offered an interesting position in Chicago.

Chappelle: Who was that?

DeGroot: My two good friends came out and visited me twice and offered a position in the endocrine section at Chicago and offered to make it--one was Ed Ehrlich, he was the junior one and the other was his boss, Richard Landau. They offered a situation that seemed very attractive because it was my own group and an opportunity to set up a program that would be more or less my own making and a promotion and a salary that seemed significant in those days. But it's so far away from significant today [that] it's hard to believe.

Chappelle: Did John Stanbury play a part in getting you that position?

DeGroot: Well, in a certain sense, he did; he thought it was a terrible idea. He thought that if I went to Chicago I would soon never be remembered on the earth again--that it was the end. [laughs]

Chappelle: But you went anyway.

DeGroot: Yes. I thought it was a good opportunity. We already had roots in the east, and we would not give up our association with the farm or New England, and we could come back. Our kids and my wife were very excited about moving to this integrated neighborhood of Hyde Park. It seemed like a much more exciting life than living in Winchester, Massachusetts.

[Tape 2]

Chicago in the late-1960s

Chappelle: You were saying that you moved to Hyde Park.

DeGroot: It was an exciting time. During the time we drove from Boston to our farm in upstate New York, the riots broke out in Chicago in the election of '68. And we watched on TV as the riots went through Chicago; it was an absolutely wild time. We were moving to that spot, and we landed there. And shortly after I started work, within a couple weeks, the students took over the administration building, and some of the faculty was asked to stay in the building even though the students had taken it over. [laughs] It was a very wild time. I don't know if you remember that, but the fall of '68 was a very, very wild time in the country.

Chappelle: Do you remember what you thought might happen?

DeGroot: I think people were--of course, it had to do with the Vietnam War and protests against the Vietnam War, but I think people were worried that the country might fall apart. It was chaotic. It's hard to imagine it, but lawlessness was significant. There were wild groups plotting [such things as] blowing up universities and government buildings and shooting people. It was pretty chaotic, pretty wild. I think we thought eventually we'd get through it, but there was certainly concern that the power of the government was being destroyed.

Thyroid Study Unit

Chappelle: Would you sketch out the Thyroid Study Unit?

DeGroot: The Thyroid Study Unit became my group--myself and researchers working with me and, then, Sam Refetoff, who joined us after a year. And we had a group of other people that worked with us. We had people in radiology, surgery, pathology, and ophthalmology, who would join us for clinical studies and evaluation of

patients and teaching programs. The thyroid group was small; it was two or three senior people and then maybe quite a few--up to ten or eleven or twelve--younger people, fellows. And then another group around it were professionals that would join us for teaching programs.

Chappelle: How was your day organized at that time?

DeGroot: Initially, when I was there, I'd see patients one full day and be involved in a teaching program half a day, and the rest of the time I would work in the lab with my fellows, either doing something or supervising something.

Chappelle: What were some of the features of your thyroid group that you particularly liked?

DeGroot: It's like running a boys' club. I had at its peak, maybe, eight or nine fellows of my own that were working on probably three different projects or four. They each had a project, but maybe there were three or four main lines of research. And so it was running a boys' club: helping people develop, finding support, and taking care of rivalries, keeping them interested and involved, and benefiting from the intellectual discussion and excitement. The best thing about it was that these were bright young guys, who wanted to go far as they could in medicine, and who were working hard as they could. So it was, intellectually, very exciting.

Lines of research

Chappelle: You said you had a couple of lines of research going on at the same time. What factors led to the lines you were working on? What choices were involved there? What was the motivating factor?

DeGroot: I became interested in autoimmune thyroid disease when I was at Mass General. And the reason was because it was very common. Six percent of women get--or maybe a little bit less than that, maybe four or five percent of women--an overactive thyroid during their lifetime. And twenty percent have thyroiditis, which is a very common condition; and of those, maybe six to ten percent become *hypothyroid*. So they're very common diseases, so I was interested in understanding the etiology--thinking of therapy--of an important common thyroid disease. So that, I think, was one. And also immunology was developing, and that was another reason. And then we had started working on thyroid hormone resistance, and so that became a central focus in our laboratory. And then, when we got to Chicago, it turned out that there were a lot of people that had thyroid cancer, [including] students and staff that we were caring for. And it was all related to the use of X-ray therapy for treating tonsil and adenoid enlargement at another hospital, Michael Reese. So we got interested in radiation associated thyroid cancer. We did a lot of research on that and on the epidemic of these

cancers, and detecting them, and whether one should detect them, and how to detect them. And that got us into the field of thyroid cancer. So there are three lines that we were in--easily, at least three.

Chappelle: One of the lines is because it was a big disease--

DeGroot: Yes.

Chappelle: And another was because it was locally right there.

DeGroot: I was dealing with these patients, yes.

Radiation associated thyroid cancer

Chappelle: So patients at the University of Chicago--those were people who had been exposed to radiation at Michael Reese?

DeGroot: Yes.

Chappelle: You tracked it down?

DeGroot: Yes. Or other places--because radiation happened to be especially used at Michael Reese, but it was also used widely. It's hard to believe it because actually the connection between radiation and thyroid malignancy had been established, certainly more than ten, maybe fifteen years earlier. But the idea that you should find people that had been irradiated and check them for cancer had never been promoted, nor was the public aware of this connection, and actually radiation was still used up to about 1959 and maybe even later for benign conditions. So it was a problem that was continuing at that time.

Chappelle: What about today with regards to thyroid cancer?

DeGroot: Well, what happened was that the topic of radiation associated thyroid cancer became very, sort of "hot topic" for a few years. And around the country, hospitals set up programs to check patients that had been irradiated, and people became aware of it. And there was a period when these patients were discovered and treated, but let us say they were treated in the 1950s, and now we're talking about the sixties and seventies. And as time went on, the treatment had been used less, especially after '59, and the patients--the onset of tumors was about ten years--commonly or so--after ten to twelve years. So that passed, and so the incidence went down, and nowadays while it still happens, radiation associated thyroid cancer is much less of a significant problem than it was.

Additional lines of research

Chappelle: Regarding mechanism of action and thyroid hormone synthesis, were you working on that before you went to Chicago?

DeGroot: Yes, we were and we continued that. That was a fourth line that we worked on. We were interested in the antibodies; we were purifying the thyroid peroxidase [TPO], and we were also studying antibodies to what was called microsomal antigen in the thyroid.

Chappelle: This was in Massachusetts?

DeGroot: Well, it started there and it continued. And then, lo and behold, it turned out that they were the same thing. The antibodies were against thyroid peroxidase. So that was quite a new and exciting finding, which we discovered, and also a group in France at the same time, actually. So we were working on purifying thyroid peroxidase [TPO] with an idea, finally--as time went on--of trying to clone it if possible--we never got there. And we were working on autoimmunity, and we investigated families with autoimmunity quite a bit; that was a big interest--the genetics. And then we got into looking at what are called T-cell epitopes: the T-cells in immune reactions respond to pieces of a protein, little short pieces. So we investigated and have for years--the epitopes that are made out of the protein that are recognized by T-cells, and we studied that. And we studied various ideas on the causation of thyroid autoimmunity: lack of suppressor cells, for example. We were pursuing several different things, and we were also at the same time working on following thyroid cancer patients, clinically. We made a registry, and we eventually collected hundreds of thyroid cases that we had evaluated, and we analyzed their natural history and their treatment and treatment methods. And we also, at this time, were heavily into looking at thyroid hormone receptors. And we actually cloned two forms of human thyroid hormone receptor, and we identified, with Sam Refetoff, the absence of a receptor in the first family that we had investigated years earlier. And we did a lot of studies on thyroid hormone receptors for the next two decades.

Laboratory tools

Chappelle: What were the most important tools that you were using in Chicago?

DeGroot: Well, that became much more involved in molecular biology: cloning, sequencing genes, looking at the factors that control the function of a gene--it's called the promoter--looking at proteins that bound to the promoter of a gene and activated the gene. So the tools were much more in the nature of molecular biology as time went on.

Chappelle: How did you go about learning molecular biology?

DeGroot: [laughs] Well, I actually took a year off in 1973 and went to France and worked in the laboratory--just did the research--but that was not so much molecular biology, it was thyroid biochemistry. But then later on, I took another short sabbatical and went back to Mass General and worked with a guy--Joel Habener--who ran the parathyroid research laboratory and learned more about molecular biology so that we could apply it in our laboratory.

Outcomes research and analysis

Chappelle: Were you taking care of patients all through this time?

DeGroot: Yes, always. I always had a good size clinical practice.

Chappelle: And did that include outcomes research and analysis?

DeGroot: For thyroid, as I said, we developed a registry of several hundred thyroid patients, and we analyzed their treatment and course, and the state of the disease when they were diagnosed, and then the method of treatment so we could look at [it]. We had patients who were treated by one kind of surgery or another, or who were given radioactive iodide treatment, or not. And we could analyze those differences. So that definitely was outcomes research.

Chappelle: Was your study unit innovative in that regard?

DeGroot: I think, actually, our first studies on the thyroid cancer patients *were* a little novel--in the sense that we introduced in that field--I think we were probably the first paper to publish data using survival curves. We had a computer program--a nice program called STATA--that allowed us to manipulate the data and analyze it and compare treatments and groups of patients. Not earthshaking; [it was] an application of something well known in other fields, but I think probably that was actually one of the early applications in thyroid. And I got deeply into thyroid cancer and its treatment for a time. We set up a National Thyroid Cancer Cooperative Treatment Study Group with about fifty members from all over the country, and we designed protocols for treatment. I tried to get money to support it from the government, which we never got. I finally gave that up after a few years, but the group persisted and still exists to this day--now, it must be twenty years later. But it's actually run now by Steve Sherman at M. D. Anderson [Cancer Center], but it is still called the National Thyroid Cancer Cooperative Treatment Study Group, and it does outcomes research using protocols for treating thyroid cancer.

X. BROWN UNIVERSITY (2005-2007) AND THE UNIVERSITY OF RHODE ISLAND (URI) (2008-present)

Chappelle: Why did you leave the University of Chicago for Brown University?

DeGroot: [laughs] Well, it was time. I must have been at age seventy or something, or more. I wanted to slow down a little bit, and I took a program that allowed me to work half-time for five years with the agreement that at the end of that time that was the end--I had to leave. I actually could have stayed on if I hadn't made any arrangement; I could have stayed forever because the rules of the university and the government were such that if you already had a tenured position, you could stay there until you could no longer function. Anyway, I wanted more free time, and so I made this arrangement for five years of half-time service, and then at the end of that five years, it was time to go. So I went. And I had a grant, so it was possible to set up an arrangement at Brown--move my grant to Brown.

On choosing Brown and URI

Chappelle: Why did you pick Brown?

DeGroot: It was in Providence, which is not too far from where our home is. That was one reason, a very good reason. And because Bob Smith, who was the head of the endocrine section there, was willing to help me. And also because my daughter was there at Brown. And I actually moved into her laboratory--took over part of her lab, one section.

Chappelle: What area is your daughter working in?

DeGroot: Well, my daughter Annie is a very bright, hard-working woman, and she's interested in a lot of things. Her research is interested in immunity--developing vaccines for AIDS or for anything else--TB, Lyme disease, whatever. And her research, in particular, involves identifying good pieces of a protein or DNA molecule for use in making a vaccine. So her research is related to vaccines and to immune responses to T-cell epitopes in making vaccines. And so the techniques that she uses, and the responses, are almost identical to what we do in autoimmunity. We're interested in *stopping* it; she's interested in *producing* it--immunity--but the techniques and the ideas are very close. We shared ideas and interests.

Chappelle: Are epitopes your main line of research right now, or your exclusive line of research?

DeGroot: Well, at this particular moment, my research is slowing down and may come to an end before long. But actually, at this moment, we are working on T-cell epitopes

to the TSH receptor and the way that they might be used in treating autoimmune disease.

Chappelle: Why did you leave Brown for the University of Rhode Island?

DeGroot: Well, I think the easiest answer to that would be that my daughter moved to URI to set up a big lab, and I moved with her over there. It was a move of a mile and easily done. It was more complicated than that, but that's a good enough reason.

XI. "THYROID MANAGER" AND "ENDOTEXT"

Chappelle: Would you speak a little bit about your Web publishing? What are "Thyroid Manager" and "Endotext"?

DeGroot: I'd love to. John Stanbury got me into books. He had edited a book called *Metabolic Basis of Inherited Disease*, which was a very outstanding book. It began with his interest in these metabolic defects in the thyroid. And when I was there at MGH, he got me to work on a book called *The Thyroid and Its Diseases*, which had been originally published in 1932, and I made the third edition in about 1964, or something, and kept that going for many years until the sixth edition, I guess. Then through John's suggestion I got interested in the endocrinology text, so we developed a textbook called *Endocrinology*, which is the best endocrinology textbook in the world, very simply put. It's called the bible of endocrinology, and it's definitely--it's outstanding, if I do say so. So I was involved in that book and the thyroid book. And the thyroid book didn't sell many copies, and it was a lot of work. And we got the idea of maybe putting it on the Web. Abbott [Laboratories] gave us some money to help do it. And so we converted it to a Web-based textbook: "Thyroid Manager"--it's not a printed book. I think the sixth edition may have been in 1995, and then about 2000--or maybe 1999, but right around that time--we put what we had at that time on the Web. And after that a group of twenty-four people responsible for individual chapters have kept updating it. So it's constantly updated, and that goes on. So the book disappeared, but the book is on the Web. It's a virtual book; anybody can print out the whole thing. And then we got the idea, well, if we can do this for the thyroid, maybe do it for endocrinology. So we set up the "Endotext," which is a complete endocrinology textbook on the Web for free for anybody in the world. To me, it has a great educational appeal; we literally get--every day--people from China, Malaysia, Indonesia, Mali, Nigeria, South America, Europe, Russia, using the site. I think that's wonderful, personally, that we can provide a really high-class source on clinical endocrinology without charging people anything.

Chappelle: How rapidly can you update?

DeGroot: About five minutes.

Chappelle: And how many authors are involved?

DeGroot: About four hundred.

XII. ENDOCRINE SOCIETY

Chappelle: Would you comment on your service to the Endocrine Society?

DeGroot: I had not been heavily involved. I was on the [Executive] Council for a short period of time a long while ago [1989-1991]. I've been on various committees, most recently on the Guidelines Committee, worked on the background for that committee, and then was on that committee. And then after that, I actually chaired the committee that wrote a guideline that came out a couple of years ago on thyroid disease in pregnancy. So I've been quite involved in that. I'm currently involved in another program, which has to do with bringing young people from abroad to the United States to work with a mentor for a year or two. It's the International Scholars Program, and I'm one of several people that helps them find their job.

Chappelle: Find a job, did you say?

DeGroot: Find a position with a mentor in this country--a laboratory.

Chappelle: What will you be doing at the meeting this year?

DeGroot: At the meeting this year? Well, I spend a lot of time at our booth, a booth that the Endocrine Society kindly allows us without cost, which is very nice of them. And we advertise our Web sites by handing out information, advertising cards, various things, and talking to people, and promoting the Web site, because even though a lot of people know about it, an awful lot don't--have never heard of it. So we're constantly trying to promote that. And I also have a poster that is on display, and I have to go to some meetings like the International Scholars presentation and meeting. But those are the things I'll be doing.

XIII. CURRENT VIEWS ON ENDOCRINOLOGY

Chappelle: What are your current views of the field?

DeGroot: Well, you know it's been a fantastic ride. I mean, to consider where we were in our knowledge of human physiology and biochemistry and disease in 1948 when I started medical school--when penicillin was brand new, and streptomycin hadn't even arrived, and we treated heart failure with kidney poisons, and research was fantastic if you did it with a chromatogram--to where we are today. I mean the increment in knowledge is so fantastic; it's been a wonderful experience. And I think anybody that's lived and worked through this particular era must feel that

way. It's an amazing thing to be--even at a low-level part--to be part of that historical advance in human biology. It's been pretty exciting.

Chappelle: Thank you.

DeGroot: You're welcome.

[End of Interview]

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Interview History— Leslie J. DeGroot, MD

Dr. DeGroot was interviewed by Michael Chappelle on June 10, 2009, during the Endocrine Society's Annual Meeting held at the Walter E. Washington Convention Center in Washington, DC. The interview took place in a conference room at the convention center and lasted ninety-eight minutes. The transcript was audit-edited by Mr. Chappelle and reviewed by Dr. DeGroot prior to its accession by the Oral History of Endocrinology Collection. The videotape and transcript are in the public domain, by agreement with the oral author. *The original recording, consisting of two (2) mini DV cam tapes, is in the Library holdings and is available under the regulations governing the use of permanent noncurrent records.* Records relating to the interview are located in the offices of the Clark Sawin Library's Oral History of Endocrinology Project.