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ISIDORE S. EDELMAN, MD

Interview conducted by
Adolph Friedman, MD
March 24, 1999

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FAMILY BACKGROUND AND EARLY YEARS

Dr. Friedman: This is Dr. Adolph Friedman interviewing Dr. Isidore Edelman in his office in New York City on March 24, 1999. Dr. Edelman, I assume I'm doing this with your permission.

Dr. Edelman: Indeed, you are.

Dr. Friedman: According to your CV, you were born here in New York. Did you have any siblings?

Dr. Edelman: Yes, I have one brother and one sister.

Dr. Friedman: What do they do now, or what did they do professionally?

Dr. Edelman: Well, they both are alive. My brother is about eighty-five. He is a retired practicing attorney. His specialty was in litigation. My sister is seventy-five. She is retired--formerly was a professor of psychology in the School of Education at Queens College, CUNY.

Dr. Friedman: Your parents--professional?

Dr. Edelman: No, my parents were both immigrants. My mother came to the United States as a young girl. She was about fifteen years of age. She came from eastern Poland. My father was about fifteen or sixteen years of age. He came from Lithuania. The only education they had was night school lessons in English, and they had some instruction in Yiddish and perhaps some Hebrew in the small town that they came from in Eastern Europe. They were both literate. They both read and wrote in Yiddish and English.

Dr. Friedman: Did your parents influence your future life and career?

Dr. Edelman: Well, when the three of us were growing up, it was simply taken for granted that we would have careers through higher education. It was never even discussed. The kind of discussion we had was which college you are going to go to and what you intended to do with your life. My mother particularly preferred that I become a lawyer rather than going to medical school. She felt that medical school was too harsh. So I'm one of the few whose Jewish parents didn't want a son to be a doctor.

INTERNSHIP AT GREENPOINT HOSPITAL DURING WWII; UNITED STATES ARMY MEDICAL CORPS

Dr. Friedman: Very unusual. Once you got out of medical school, did you go right into the Army?

Dr. Edelman: I did an internship at Greenpoint Hospital [in Brooklyn New York] during World War II--it was only a ten-month internship. And then I was inducted in the Army as a first lieutenant in the Medical Corps.

EARLY INTEREST IN PSYCHIATRY

Choosing between psychiatry and internal medicine while in basic training; training at Fort Mason General Hospital in neurology and psychiatry; caring for neurological and psychiatric patients at Fort George Meade

Dr. Friedman: Once you got into Army life, how did you end up in psychiatry?

Dr. Edelman: Well, I was interested in psychology in college. And I had been thinking about either going into psychiatry or internal medicine--I wasn't sure which--while I was in basic training in the Carlisle Barracks. Early in 1945, there was a call for volunteers to go to a training course in psychiatry and neurology at the Fort Mason General Hospital on Long Island. I thought that would be preferable to being a battalion aid surgeon. I didn't see myself in that role being especially effective. I was accepted. We spent about eight weeks at Fort Mason--essentially being instructed eight to ten hours a day--and at the end of those eight weeks, we were declared both neurologist and psychiatrist. I was assigned to the General Hospital in Fort George Meade and cared for patients with both neurological and psychiatric problems.

CHOOSING A CAREER THAT COMBINED BASIC RESEARCH AND CLINICAL INTERESTS

Difficulty in finding a position following discharge from the Army

Dr. Friedman: When you got out of the Army, you went into neoplastic classes of diseases. That was the only residency you could get--or because you chose?

Dr. Edelman: I already had a taste of psychiatry and neurology. When I was in the Army, I did a little documentary study, [which] was published. And I always had an interest in research. I decided what I wanted to do was to combine my clinical interests with a research career. I explored whether there were training programs in psychiatry [that] included research options. I contacted Langley Porter Clinic in San Francisco, the clinic in Kansas, and the psychiatry department in Cornell. I would say probably half a dozen of the leading departments in psychiatry. They all had clinical training programs and--in 1947--none of them had a research program. So that led me to abandon the thought of going into psychiatry--because my experience in psychiatry in the Army indicated that most of what was the nature

of psychiatric disorders were simply untreatable. What was needed really were newer initiatives. But I was getting out of the Army at the time when there were a lot of MDs coming out looking for clinical training. I had quite a good educational record; I was an AOA in my class--one of the top students. I think that I graduated fifth in my class out of about one hundred and ten. I had excellent letters from the dean of Indiana University, but every place I applied to for a residency in medicine turned me down.

MONTEFIORE HOSPITAL

Gaining a residency through the assistance of Boas and Bluestone; externship in the neoplastic division under Daniel Laszlo; chief resident of neoplastic diseases; postdoc fellowship with Louis Leiter

I got to Montefiore by a very indirect route. It turned out that--I was doing some of my research at the Gorgas Library, as I was stationed in Panama--the librarian was a friend of the distinguished physician in New York, Dr. Boas. He was a friend of the director of my Montefiore Hospital. She wrote to Boas on my behalf telling him she thought I was worthy of being given support, I had a good academic record, and couldn't get any residency training. So Boas contacted the president at Montefiore--who was Bluestone. Bluestone and Boas contacted me. I sent them summaries of my records. Dr. Bluestone then said, "Well, we don't have a residency vacancy, but we can give you an externship which would initially have no salary attached to it in the neoplastic division under Dr. Daniel Laszlo." I accepted that for--and the first six months, I was an extern. The next six months, I was chief resident of neoplastic diseases; the following year, I spent with Louis Leiter as a postdoc research fellow in medicine.

Dr. Friedman: When you were at Montefiore, by chance did you ever meet Samuel Seidlin? He was in nuclear medicine.

Dr. Edelman: I don't remember him.

Choosing an academic career and basic clinical research

Dr. Friedman: After you had spent a year with Louis Leiter--was there anything great about the year?

Dr. Edelman: My experience in Montefiore was terrific. That's what convinced me that I really should proceed to follow an academic career. It introduced me to a high level of basic clinical research. Both Laszlo and Leiter had programs. Leiter had a more advanced program--more funding and more opportunities--that introduced me to the major scientific meetings like FASEB [Federation of American Societies for Experimental Biology and ASCI [American Society for Clinical Investigation], AAT meetings. It started me in doing experiments and in writing papers. That convinced me that I should stay in fulltime academic work.

AEC FELLOWSHIP IN FRANCIS MOORE'S LAB AT HARVARD

Using radioisotopes; building a Geiger counter

I applied for and got one of the first AEC [Atomic Energy Commission] fellowships to work in Francis Moore's lab at Harvard because that was one of the few laboratories that were using radioisotopes in medical research, which was very sophisticated in those years. You had to build your own Geiger counter.

Using isotopes to measure quantities of water, sodium and potassium in the body; developing interest in the dynamics of water and ion distribution; quantifying distribution of water, sodium and potassium

Dr. Friedman: What did you do in Moore's Laboratory?

Dr. Edelman: There were two main foci to my work. One had to do with body composition--because the isotopes gave you the opportunity to measure quantities of key constituents like water, sodium and potassium in the body; whereas prior to that time, you could only measure balances. That was a continuation of the work that Dr. Moore started. He was one of the pioneers in usage of isotopes, both stable and radioactive, in measuring the major constituents of the body--and indirectly from water measurements, estimates of lean body mass. In addition, I became interested in dynamics of water and ion distribution--because no individual is invariant with respect to body composition. I became interested in how to quantify the rates of distribution and the regions of distribution of water, sodium and potassium. That also related to my early interests in salt and water metabolism and clinical things that I did with Leiter. I continued that work in a different way when I went to the University of California in San Francisco. We had new ways to measure both transition state and steady state quantities of sodium, potassium, and water in the body. That led to some new information about variations on body compositions when the serum concentrations were abnormal.

CHOOSING ENDOCRINOLOGY

Dr. Friedman: Sounds like a tremendous bit of work!

Dr. Edelman: Well, I was busy. My interests in those topics led me into questions of what regulates these systems, and that got me into endocrinology.

Dr. Friedman: I see you were in California a fairly long time.

Dr. Edelman: Twenty-six years. I spent two years at Montefiore, four at the Brigham at Harvard, then twenty-six years in California. Now I'm approaching the end of my twenty-first year at Columbia.

BIOCHEMICAL MECHANISMS

First efforts in endocrinology: gastric mucosa as a means to study the biochemistry of steroid hormones

Interest in regulatory activity of ion transport

Dr. Friedman: When you got into endocrinology by virtue of all of these balance studies in electrolyte situations, did you go right into adrenal disease?

Dr. Edelman: Well, I never was involved in clinical endocrinology, because by then my interests were in biochemical mechanisms. I did for a time think that I could use the gastric mucosa as a model for the distal segment of the kidney--because the gastric mucosa absorbs potassium and secretes sodium, water, and hydrogen, [as] does distal tubule. We knew that steroids had a powerful influence on salt and water balance because the most prominent features of Addison's disease are electrolyte disturbances. So my first effort in endocrinology was to see whether the isolated gastric mucosa could be used as a target to study the biochemistry of the action of steroid hormones, particularly glucocorticoids or mineralocorticoids. At that time, it was easier to get synthetic steroids than aldosterone in a natural form in sufficient quantities for experiments. So my first experiment on gastric mucosa might have been done with hydrocortisone. We published a few papers on ion transport across the gastric mucosa. I was really interested in regulatory activity.

Toad bladder as a model system to study the biochemistry of aldosterone
Roy Maffly establishes that aldosterone regulates sodium transport across the mucosa of the toad bladder

In the early sixties, Jean Crabbé published a paper on the ability of aldosterone to augment sodium transport across the isolated toad bladder, and [that idea] had been introduced by Alexander Leaf. Leaf realized that a structure that behaved like the distal segment of the kidney could be a valuable model system, and Jean Crabbé--working in Leaf's laboratory--reported that aldosterone augments active sodium transport in this system. A fellow in my lab, Roy Maffly, had previously worked in Leaf's lab, so he was the connection between the two labs. And Roy followed up on Crabbé observations and satisfied me and everybody else that Crabbé was right: that aldosterone did regulate sodium transport across the mucosa of the toad bladder. That put us full time into the use of the toad bladder as a model system to work on the biochemistry of aldosterone.

CHOOSING TO ACCEPT THE CHAIR OF BIOCHEMISTRY AT COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS

Working on molecular mechanisms rather than organismic types of physiology

Dr. Friedman: What made you leave California to come East?

Dr. Edelman: Well, I was fifty-seven at the time. I was by now completely committed to working on molecular mechanisms, rather than more organismic types of physiology. Until that time, I avoided any major administrative responsibility. I was offered the chair in biochemistry at Columbia University College of Physicians and Surgeons. That appealed to me for two reasons: One is it added a new dimension to what I was doing, but it was compatible with continuing to run a research lab, which had been my main focus of activities for a long time. The other reason was that the department of biochemistry at Columbia had a particularly distinguished history, which appealed to me a great deal. That is the historical context.

Feelings about administrative work

Dr. Friedman: I have noticed from your CV you are intermittently involved in an administrative role. Did you enjoy that work, or did you tolerate it as a matter of that's how you can get where you want to go?

Dr. Edelman: I guess I always had the feeling that there were some rewards possible in administration. I served for two years as chief of medicine at the San Francisco General Hospital on the University of California Division. The Hospital had both the Stanford Division and UC Division, but I soon realized that if I stayed on as the chief of medicine, it would probably impair my work in the laboratory. So when Comroe came to be head of the new Cardiovascular Research Institute at Columbia--

Dr. Friedman: Julius Comroe?

Dr. Edelman: Julius Comroe. I made it clear to him that I wanted to spend more of my time in research than was allowed by serving as a chief of medicine of a large clinical program. He invited me to become one of the staff members in the Institute. The Department of Medicine, which is where I held my faculty position, invited me to run the renal and electrolyte service. In the middle of the sixties--around '66, or '67--I was offered a professorship elsewhere. I told Comroe and Holly Smith that if I had full time for research, I would give up my responsibilities as head of the service in the Department of Medicine. They offered me a research chair. About the same time, Comroe asked me to serve as an associate director of the Cardiovascular Research Institute. But that involved very little work. Julius was a complete academic administrator. And Dick Havel and I, who were the

associate co-directors, would meet with Julius in his office--maybe once in two weeks or once a month spend an hour talking over things--and that was the extent of our work. I never had major administrative responsibilities, except for the short time I was chief of medicine at the San Francisco General and [the] eleven years I spent as chairman of the Department of Biochemistry at Columbia. It happens that the last few years I have been director of the Columbia Genome Center.

THE COLUMBIA GENOME CENTER

Dr. Friedman: That was my next question--I have two questions: One, how do you get into it? And two, does just being a director augment or interfere with your ability to do research?

Early interest in a genome initiative

Dr. Edelman: Well, by 1968, I spent eleven years as chair of biochemistry and molecular biophysics. In the late eighties, I was more interested in active transport mechanisms than in endocrine mechanisms. But I wasn't really inspired by what I was doing. I thought I was doing good work. I didn't see the point of my staying in that field until I was seventy-five or seventy-six and then fading out. I wanted to find something that would be more challenging. Just about that time, the steps taken by a group of molecular biologists to create a genome initiative got my attention. My immediate reaction was that this is the wave of the future. Even though I knew very little about genetics, I knew a little about molecular biology because I was using those methods to study hormone action.

Leaving biochemistry and transport systems; creating a genome program at Columbia; converting a program to an authentic center; discovering new genes implicated in disease states

Dr. Friedman: You also had great foresight.

Dr. Edelman: Well, perhaps. I leave that for others to say. But I knew that I could have an impact on genomics and that my administrative experience would enable me to survive when the young tigers came to chewing my tail. So in 1989, I essentially ended my work on biochemistry of transport systems. I persuaded one of the senior molecular biologists, Argiris Efstratiadis, to join me in creating a genome program in Columbia. From 1990 to 1996, the two of us ran the genome program at Columbia. In 1996, I decided that it was time to convert what was a program at Columbia to an authentic center. At Columbia University, a program exists only as long as there is external funding. We had got funding for six years, but we were not a center. And in 1996, I persuaded the provost and the vice president for health sciences that it was time to create a genome center. I served as the first director, which we established in that year. We now have a comprehensive

genome center. We have 22,000 square feet of space and about forty-five scientists working in the center--organized in seven sections--and an annual budget of about four million. The orientation of the center gives me particular pleasure because it takes me back to my clinical roots. Rather than doing just large-scale sequencing without regard to biology, we're focusing our attention on discovering new genes that are implicated in disease states. In the summer of the year 2000, which is the month in which I'll become eighty, I will step down as a director, and Conrad Gilliam, who now heads the Molecular Genetic Section, will succeed me. He is now the co-director, and we'll work out a seamless transition. We have a portfolio of clinical projects ranging from manic-depressive psychiatry, to retinitis pigmentosa in the eyes field, to hematological cancers.

Dr. Friedman: That was fascinating.

Dr. Edelman: So I'm very pleased with how the center worked out and where it is going. When I step down it should have about seventy scientists working in the center.

Dr. Friedman: You do--

Dr. Edelman: No, not that soon. That would be in five years. I should say by the year 2000 we would have about sixty or seventy scientists working.

Funding issues

Dr. Friedman: Do you have a lot of trouble getting money?

Dr. Edelman: Getting money is always a challenge. We handle this in a variety of ways. One of the main pathways is applying for NIH grants, but we raised six million dollars in philanthropies, and we got about eight million from industry. We also have some New York State funding--a variety of sources like that--and the University puts money into it.

ENDOCRINE SOCIETY

Dr. Friedman: It's great! I'm changing my questions a little bit. You got a few awards from the Endocrine Society.

Dr. Edelman: Yes.

Dr. Friedman: And yet your contact with the Endocrine Society wasn't great.

Dr. Edelman: Well--

Dr. Friedman: The awards were for your accomplishment in sciences.

Dr. Edelman: Right. I did serve on the council of the Endocrine Society, so it wasn't completely at arms length. I forgot the year.

LAURENTIAN HORMONE CONFERENCE; GORDON CONFERENCES ON HORMONE ACTION

Dr. Friedman: And you also served on the Executive Committee of the Laurentian Hormone Conference.

Dr. Edelman: Yes, for about five years, and I participated actively in that program. I also participated very actively in the Gordon Conferences on Hormone Action.

Dr. Friedman: I'm not familiar with it.

Dr. Edelman: The Gordon Conferences are research meetings held a week at a time--in those years, usually in New Hampshire. They are specialized meetings. For a time, I was pretty active in participating in and organizing Gordon Conferences on Hormone Action.

Dr. Friedman: Is there anything else I should know about you or what you've done that I didn't ask you about?

HONORS AND AWARDS

Dr. Edelman: Late in life, I got some awards that I hadn't expected. I don't know even if they appear on my CV.

Dr. Friedman: I'm up on the '99 A. N. Richards Award.

Dr. Edelman: Yes, there is one more since then. I just agreed to give the first Mortimer Sackler Medical Research Lecture at Tel Aviv University. That will be in June of this year.

MARRIAGE, FAMILY, AND CHILDRENS' CAREERS

Dr. Friedman: Another thing I didn't get involved with is about your own family--I neglected to ask you about your family. When I called your apartment there was Dr. Ross and Dr. Edelman.

Dr. Edelman: Dr. Ross is my second wife. My first wife and I had four children. We were divorced in 1974, and at that time we'd been married for thirty-two years. The four children are all successful in their own fields.

Dr. Friedman: What were their fields?

Dr. Edelman: Well, my oldest son is an associate professor in the Department of Pharmacology at the State University of New York in Buffalo. He is on the editorial board of the *Journal of Biological Chemistry*--successful in his field. The next one is a girl who is an independent contractor in Hollywood as a casting director. The next one is a boy who is an analyst and fund manager in biotechnology. The youngest is a girl who is a tenured school psychologist in the Berkeley School District in California. They all have advanced degrees and [are] financially independent.

Dr. Friedman: Particularly, the financial advisor.

Dr. Edelman: Well, he is a financial manager. Yes, he is. Well, my older daughter is pretty well off, too, because her husband is a director and a producer, and between the two of them, they make plenty. My second wife, Roslyn, has one daughter. She and her husband are very successful in the computer field. They invent and manage software packages for hotels and resorts.

Dr. Friedman: Those are tremendous fields.

Dr. Edelman: They are very successful. So the only trouble I have is I worry about some of them becoming Republicans

Dr. Friedman: What is your wife doing?

Dr. Edelman: Roslyn is a tenured faculty member in the same department as my younger sister was before she retired, which is in the School of Education at Queens College, a part of the City University. She does fulltime teaching and has her own research and interests.

Dr. Friedman: They're a wonderful family.

Dr. Edelman: Well, I'm pleased with them.

Dr. Friedman: You should be. I want to thank you very much for all the time you have given me.

End of Interview

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