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Harvard Medical School (1958)
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Lillian Welsh Memorial Award, Goucher College (1951)
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Honorary Degree, Goucher College, Maryland (1993)
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Susan Leeman's research has focused on the two peptides, substance P and neurotensin, which were isolated and chemically defined in her laboratory subsequent to her detection of a sialogogic and a vasoactive substance in hypothalamic extracts. The determination of their amino acid sequences and the synthesis of these peptides have opened up fruitful fields of research for many investigators. Her recent work has explored the roles of these peptides in the inflammatory responses of various tissues.

Susan E. Leeman

I have found the task of writing my autobiography rather daunting, as I am not sure how finished I feel my life is or what it has all been about. I have conflicting and changing thoughts about my experiences, and particularly about how private to keep them. My career path has been laced with feelings from my own psychological development; and, surprisingly at my age, I continue to feel impaired by having been brought up in a sporadically dysfunctional family. How much to attribute my many times of uncertainty about my professional course to the institutions in which I have found myself working, or to general societal attitudes toward working women, and certainly women in science, and how much to attribute to my own personal issues has been a problem for me.

Whether my reflections and the recounting of my experiences will be of value to other scientists who may have periods of doubt themselves is not clear. Maybe there are others out there whose motivation has occasionally flagged, and even whose feelings have sometimes been hurt. But, on balance, I feel that there have been many rewards; and I would like to declare that, overall, I finally feel that I was worth the investment. I would like to encourage others to persevere, if they want to.

So here goes.

Early Years and Influences

I was born in Chicago in 1930. My father was a metallurgist for the U.S. Steel Company in Chicago, a job he took after leaving the Bureau of Standards in Washington. My father was a scientist with very high standards, and he was a very academically driven person. When he was 9 years old he won a medal from the *New York Times* for an essay on Abraham Lincoln. I came upon it in junior high school in a bureau drawer. I never spoke to my father about his prize.

My mother attended Hunter College during the flapper era. This was somewhat surprising as not many women went to college in those days. My father was 10 years older than she, and he could be very intimidating—an academic tyrant. He did not think my mother was particularly smart, although I could sense that she was.

My father's family had emigrated from Russia to New York City when he was barely 7 years old. They were a very striving people who had been persecuted in the country they had left and wanted to do well in their new country.

My father was always grateful for the opportunities that the United States had to offer; for example, he felt that paying income taxes was a privilege. He had two brothers and a sister. One of his brothers became a teacher, the other a patent lawyer, and his sister also became a teacher and a very successful poet.

I always felt myself to be a somewhat peripheral and unimportant member of the family. I had one older brother, Henry, who was born in Washington, D.C., when my father was working for the Bureau of Standards. Things were expected of my brother, but not much was expected of me. I concealed an inner "how about me?" attitude because of this, which I believe continues to this day. I did not and do not want to be overlooked, but I have found it hard to be a serious academic. I have always known that I have a very silly side.

My mother's mother, Grandma Gittel, was from a fairly large estate in Vitebsk, Russia, the same place that Marc Chagall was from. There were no public schools. Her father had hired a tutor for the boys, her brothers, but not for the girls, and she took issue with that. At age 13, she stole money from her mother and bought a ticket to Odessa, a two-and-a-half day train trip away, to go live with relatives. She knocked on their door, explained who she was, and they took her in to be a babysitter and household help. She never saw her parents again, and that was certainly part of her lifelong depression.

The relatives in Odessa also had a dairy business that was run from their house, and my grandmother was soon incorporated there as a helper. Because she was so smart and hardworking, at age 15 she was given a cow of her own. She went on to develop her own route and create a successful business without being able to read or write. Years later, when she lived with us in Bethlehem, Pennsylvania, she used to tell me how frustrating this was for her. She had used hieroglyphics to keep the accounts of her dairy route. She would draw on a piece of paper the particular characteristics of each house; for example, a broken fence, or an asymmetric placement of the windows. With this system she was able to keep her records, make correct deliveries, and flourish as a dairymaid.

After several more years, the family began to worry about her future. She was getting older and the prospect of her becoming an old maid was fearsome. After all, she was 22 or 23! When she met a big burley, dashing Jewish soldier in the Russian army, the family advised her to accept his offer of marriage. Their words of advice to her echoed in my ears when, years later, it came time for me to consider getting married: "Who knows, maybe nobody will ever ask you again."

She once confided in me that she hardly had known him and had considerable misgivings about the match. But, they were married; and she and my grandfather lived in Odessa for several years. There they had a baby who died. Then, around 1903, my grandfather was told that he would have to fight in the Russo-Japanese War. He decided to run away to the United States instead. He and my grandmother made plans to reunite in New York City.

My grandmother traveled by herself to Hamburg am Bremen and booked passage on a very crowded boat to the United States. She said it was a miserable trip with many seasick passengers. She landed on New York's East Side, located my grandfather, and they began life together in the new country.

My grandfather was a boisterous man who loved music, sang Italian arias at the top of his lungs, learned to speak Italian before English—because that was the neighborhood they were living in—and earned his living as a customer-peddler. Eventually, they moved to the Bronx and had six more children. My mother, the eldest, was heavily relied upon as a housekeeper and babysitter. She was also an excellent student, graduating at the top of her class. After graduation, her father wanted her to work in a hat store. But she wanted to go to Hunter College, which was a free public school in New York. My grandmother, who had had a similar problem with her own father, supported my mother's education and won. So my mother went to college!

After her first year, a school friend introduced my mother to my father. She was 19 years old; he was 29, a college graduate, and already started on his career. My father lived in Brooklyn and she lived in the Bronx, and there was a definite attitude on my father's part as to who were the peasant immigrants and who were the striving immigrants of cultural superiority. My father was a Litvak—taller, blonder, more intellectual, and, in his mind, of a superior quality to my mother's family. That was always a bit of a struggle.

My father went to City College and, when he was drafted, he was sent to Carnegie Tech in Pittsburg because he was also very smart and wanted to be a scientist. He got an education in the emergent field of metallurgy, which was of military-industrial value.

When he proposed, my mother accepted, partly to get away from home. It was 1918, and the war was over. He was then employed at the Bureau of Standards in Washington, D.C. She transferred to George Washington University and graduated from there, shortly before my brother was born in 1928. Soon, my father was offered a job at the U.S. Steel Company in Chicago, where I was born 2 years later.

When I was 6 weeks old, we moved to Columbus, Ohio, where my father accepted a job at the Battelle Memorial Institute. The focus there was more on research than his previous position had been at U.S. Steel, and he enjoyed this. But after 6 years there, the family story is that he was informed by the Battelle administration that, because he was Jewish, it was unlikely that he would advance much farther in his career there. He was still academically ambitious, so he decided to accept a job at the Bethlehem Steel Company in Pennsylvania. We moved to Bethlehem in 1936.

Somewhat before the World War II, there were very serious strikes in the steel industry. The Council of Industrial Organizations was getting the steel workers to organize. My father's position as a researcher was neither management nor labor but somewhere in between. He felt it was very tenuous.

Bethlehem was also largely anti-Semitic. We were not allowed to join the country club; and we knew that we were second class. I remember when

I was elected president of the seventh grade and a classmate, Danny W., shouted, "Hey, Jewface!" at me from across the room. I had thought that my high office had spared me from that kind of thing. We forget what a bigoted country we have been for a long time.

Well, we joined the public country club.

My mother's mother moved in with my family in Bethlehem when I was in the fourth grade. Her sons were drafted in World War II, and she could not support herself. My father was a fairly well-recognized metallurgist by this time, and we lived a middle-class life. When she needed a place to live, he said that she could come stay with us.

My grandmother and father got to be good friends, and I think my mother was very jealous. He used to read aloud to my grandmother the Sholom Aleichem stories about the shtetl, and other tales from the Lower East Side. They seemed to be revisiting the old country together, enjoying the safety of being Jewish in our living room. I can remember the look on her face when Khrushchev came to the United States and took off his shoe and banged it on the desk at the United Nations. She had a look of such nostalgia to be hearing Russian again on the radio.

Meanwhile, my grandmother's relationship with my mother was deteriorating. My brother and I could never figure out why. My mother was becoming more and more incapacitated. During the war, she was volunteering as a nurse's aid, and had gone back to school to take a course in ferrous metallurgy so that she could get a research job at the U.S. Steel Company. She was a technician of sorts. On V-J Day, my mother was fired. All the women who had joined the workforce were gone, without exception. She took it badly.

My grandmother had also displaced my mother's role in the house. After my mother was fired from her job, two women in the household became too much. Eventually, she exploded and ordered my grandmother out. Then Grandma Gittel went back to New York to live with one of the other children.

I think that my grandmother knew when the Russians killed her family back home. There was a lot of slaughter of people, but those who got to the United States were mostly O.K. We heard about the gas ovens in Europe and that millions of people were being murdered. I do not know how people in Germany claimed they had no idea what was going on, when I knew in Pennsylvania. Delegations of Jews were going to see Roosevelt to beg him to bomb the railroad tracks leading to the gas ovens, and he would not do it.

During the war, my father was very anxious. Although he was an American citizen, I think he could not be sure that he was going to be safe. The Pope never spoke out against the slaughter of the Jews, so we could not count on the church. I think I picked up this anxiety too. I can remember thinking on my way home from school, "Where would I hide?"

Bethlehem was full of people from Romania, Poland, and the Eastern European countries, which had been the most efficient at slaughtering the Jews. We lived in the Christmas city of the United States, and the Jews were

thought to be Christ killers. That was another thing that would be shouted at me in school.

I can remember when my daughter Eve was invited to sing in a church at Christmas in Newton, Massachusetts, and I thought, "What?!" I had been petrified just to walk into a church. It is probably something like what Muslims feel now in our country.

I spent a lot of time as a child raising money for Israel. My mother made me go around the neighborhood selling movie tickets door-to-door. It was considered very important that there be a country for the Jews, but I hated this task. Now I look at Israel and think, "How can you be so treacherous? What are you doing building walls?" But then we thought somehow that it would spare us from anti-Semitism. Today, I continue to have mixed feelings about Israel.

In those days, Bethlehem seemed against most things that you could think of. I remember the family drama that ensued when my Aunt Molly, my mother's sister, married Paul Robeson's bodyguard, Homer Sadler, a Black man. Molly and Homer had two daughters and many grandchildren, all of whom have gone to college. When I went to the Endocrine meetings in California to receive the Koch Award, my uncle took me to the horse races. He would bet and he always made money, and my Aunt Molly did not like this at all. They were a fun side of the family for me; but my parents were unable to accept that she had married a Black man. My mother was afraid that if they visited us in Bethlehem that the neighbors would see him, and that somehow this would hurt my father's position at the Bethlehem Steel Company.

Later at Harvard graduate school, when I encountered discrimination against women wanting to become scientists, I did not think of protesting or objecting to this biased treatment even in my heart of hearts. I think this was because I had lived so many years in Bethlehem accepting discrimination as a way of life.

Looking for escape as a youngster, I consented to attending Hebrew School, and joined the Girl Scouts. As a teenager, I tried to get out of the house whenever I could, especially summers when my father took his 2-week vacation. My parents often quarreled then with great bitterness.

I became inseparable from my best friend Nancy Schrader. We lived near each other. She was the youngest child of a Pennsylvania Dutch family and she was not Jewish. Her father did not approve of me. I remember a story at Christmas time when her father came down the stairs and wished her a merry Christmas and she replied, "Bah, humbug!" and he said "You are not to play with that Susan Epstein anymore!"

Nancy and I used to laugh ourselves silly. She was really a good friend. When we were in high school, we would play hooky a lot. I can remember going to see Ingrid Bergman in *Casablanca*. Here was this new Swedish star! I would steal money from my mother, and we would pay adult prices so

no one would know we were kids. Our other friend Sylvia had a car, and we would drive for miles, sometimes halfway to Harrisburg. We would go swimming in the creek and have other adventures.

Because of her poor grades, the guidance counselors at my school tried to help Nancy, while I, who really needed help, was ignored because my grades put me near the top of the class. I was a straight-A student but could not commit to anything in particular because I was interested in so many different things. I was in several school plays and toyed with dreams of becoming an actress. I always knew that I did not have a life plan, and I still don't. I just knew that I wanted to get out of Bethlehem at some point, so I figured I had better apply to college.

My brother was living at home and going to Lehigh University at that time. Sometimes I would go to his fraternity parties. There were no girls' colleges within commuting distance, so I ended up applying to go away to Goucher College in Maryland.

I went with my father and brother to the interview at Goucher; and they talked to the admission's officer the entire time. I did not say a word; and I remember thinking, "Gee, why did they bring me along?!" But I was accepted, and I went.

Goucher at that time was a women's college that supported the notion that it was acceptable for women to want to think seriously about things. Being in an all-girls' school made participation in class discussions more comfortable.

I decided to major in physiology, which was unusual at the undergraduate level, and it was only offered as a major at Goucher because of unique circumstances. The Chair of the department, Phoebe Crittenden, had been turned down for tenure at George Washington University Medical School. In those days, there were almost no women on medical school faculties. She gave up wanting tenure, but because she wanted to stay in the area, she created the undergraduate Physiology Department at Goucher. I remember her as a nice woman—although I did not want to view her as a female role model. She was unmarried, lived with her dog, and seemed to have had to give up her femininity to survive in the academic-medical environment.

At Goucher, I became good friends with my roommate, Francis Hackett. She was a history major, who, later with her husband, went on to establish a highly respected and profitable publishing company, The Hackett Publishing Company.

I remember one day coming back to the room after class, and Francis said to me, "You look really terrible today. You look just like a science major." That did give me pause.

In my senior year, I had the nerve to try out for a part in a play that was to be presented at Goucher, Aristophanes' "The Birds." I was given a funny part, and the drama coach asked if I had ever thought of going on the stage. I said that I had. She said she would not suggest going into theater for my

looks, but that I had a funny sense of comedy. Her comments lasted with me for quite a while, and later when I had a talk with my father about what my life plans could be, I shyly told him that I sometimes thought of an acting career. He said to me, "Well, if that is what you want," with a slight tone of desperation. The option was always in the back of my mind.

When I graduated from Goucher, I went to live with my Aunt Eunice and Uncle Sam in their New York City apartment on Riverside Drive. I think they expected me to be something of a babysitter. My Aunt Eunice deConti was an accomplished Brazilian violinist, and incredibly talented groups of musicians and ballet dancers would come traipsing through the apartment. That was where I really had my first lessons in music criticism. I once treated my aunt and uncle to a concert at Carnegie Hall, and my aunt turned her critical judgment on the violinist. She said that he had no talent and that he was not even playing in time. She was devastating, and so incredibly sophisticated. I could see why she later became so well respected and important in the music life of Sao Paulo. Eventually, my grandmother got over the fact that my Aunt Eunice was not Jewish.

My aunt had won a scholarship from the Brazilian government to study at Yale. She spent a summer at Tanglewood and that is where she met my Uncle Sam, a music lover who had been discharged from the U.S. Coast Guard. They got married in San Paulo and came back to live in New York; but my aunt did not like American family living because there was not enough focus on family contact.

The summer I went to New York, I accepted a job as a technician working at New York University (NYU) in the laboratory of two clinicians, Herbert Chassis and William Goldring. Their project did not interest me. It seemed to have no rhyme or reason, and I was unimpressed by the quality of the science. They were just doing endless renal clearances on very sick patients who had been treated with nitrogen mustard. There was not a hypothesis in sight. After doing these analyses, the results would be tacked on the wall. Chassis would walk in, throw his camel's hair coat on a chair, put his feet up on the desk and say, "My how the data seems to accumulate!"

I began to get intellectually restless. One of the perks of the job was that I was allowed to take courses at night at NYU. I studied the history of mathematics. It was a very well taught and interesting course. Then I started to get the idea that maybe I would like to go to medical or graduate school. I had not taken any organic chemistry yet so I enrolled in another night course.

I met my friend Jean Blumberg at NYU. She had had the job the year before and she taught me to do the inulin assays, which was the methodology used to measure the renal clearances. We got to be friends then, and we still are. That summer, when she suggested that we go on a youth hostel trip to Europe together, I was happy for the adventure.

When we returned from Europe, I think I had some of my grandmother's worry that I was getting old and that it was time to get serious, settle down, and get married. I remember thinking, "Someday I will be 25, and *then* what am I going to do?!"

Graduate School and Career Beginnings

That fall, I went to live with Jean Blumberg's family. I worked as a technician at the Rockefeller Institute and took various philosophy classes at Columbia University at night. I studied Aesthetics with Irwin Edman, and attended John Randall's course in the History of Philosophy. However, I soon realized that I had no particular talent as a philosopher, nor did I care to turn my mind to such questions as, "When is a sentence not a sentence?" I figured, "Maybe I had better go measure something!"—and that meant going to graduate school.

My brother was getting his doctorate degree at the Massachusetts Institute of Technology (MIT) in Cambridge, Massachusetts, so I applied to graduate school at Harvard to be close to him and to explore another city. I assumed I had applied to the graduate school in Cambridge, but they sent my application to the medical campus in Boston where they were starting a brand new program emphasizing basic medical sciences. I qualified for this because I had been a physiology major as an undergraduate at Goucher, and this subject was taught mainly at Harvard Medical School.

Because I hated filling out the forms, I applied to only one graduate school. Harvard accepted me, but my academic program was administered through Radcliffe. There, we were a group of 13 students. We spent all day every day together. There was a lot of faculty tension because the professors who were assigned to teach were temporarily shunted aside from their main career track at Harvard Medical School. The students did not like it because we were an odd mix of people. There were four top-of-the-class medical students mixed in with the rest of us graduate students, and we were very different kinds of people. The medical students memorized everything, whereas the graduate students endlessly questioned methodology. What I disliked most was the constant contact with the same, small group day after day.

We were part of an experiment on how to revise medical school curricula through a grant from the Commonwealth Foundation; but we were not even the right subjects. It was odd. It was a one-year program, and I could not wait to get out of there. I took pottery classes at night.

At the end of that year, we had to pick the department we wanted to enter. I had problems with that because I had had a miserable time at graduate school and was considering applying to medical school. I applied and was accepted to NYU, but then I had reservations. I did not want to take the spot away from someone else who really wanted it.

Ultimately, I decided that I did not want to take care of sick people. My mother had taken a course in nurse practitioner during World War II. She and later my daughter who went to medical school to become a psychiatrist were far more interested in caring for the sick; but it was not for me.

During graduate school, I was engaged to the son of a well-known Italian composer. My fiancé was drafted during the Korean War and sent to Alaska. I had been a bit swept off my feet by his elegance, although I had reservations about him being a Republican. He was actually pro-Nixon! When he was drafted, I was sort of stuck thinking, “Well, now what do I do?” So I stayed in graduate school with the idea that it would just be until he came back.

When it came time to choose which department to go into, what really mattered to me was that I had to like the person I was going to be working with. The Physiology Department at Harvard just seemed so stodgy, autocratic, and old-fashioned. But then I met Dr. Paul Munson in Pharmacology. He was working in this new area called neuroendocrinology and was one of the few professors interested in it.

I thought neuroendocrinology was intriguing because it offered an anatomical pathway by which emotions, thoughts, and feelings could travel through the central nervous system (CNS) and connect to the anterior pituitary gland to regulate the release of many hormones from the anterior and posterior pituitary glands. These hormones are then secreted to the rest of the body. This pathway explained how many peripheral physiological responses could be mediated by emotional stimuli.

Although I was interested in physiology, I was particularly interested in questions of the mind–body bridge. I was taken by the idea that some specialized nerve cells in select places in the brain not only function as nerve cells but also function as endocrine cells. They are true neurons in that they can accept and transmit electrical stimuli, but substances released at their terminals are passed—not onto the next neuron—but rather, into the vasculature. Their transmitter agents are released into blood vessels, and they reach a distant target by way of the circulation.

I asked Dr. Munson whether he would consider taking me on as a graduate student, and he agreed. He was a socialist, and I loved that. He was also a jazz lover, and he was very supportive of his wife’s career as a researcher. In fact, he was so pro-women that when I was getting married, he tried to talk me into keeping my maiden name.

Dr. Munson and I were friends until the end of his life. I was honored to speak at his memorial as one of the few graduate students that he ever had. He was an important influence in my scientific career. He impressed upon me the value of a bioassay, the basis of my two discoveries. As the years go on, I am more and more impressed with the value of a good bioassay, and the need not to drift too far from the dock.

If it had not been for Dr. Munson, I would not have stayed in graduate school—at least not at Harvard, which at the time, in my opinion, provided

a dreadful atmosphere in which to educate young women scientists. In my class of 13, there were 4 women. One, Biljana Nikitovitch-Winer, left the medical sciences program after receiving a failing grade, earned a degree from Anatomy and later became the Chair of an anatomy department. The circumstances of her failure were absolutely unfair. Another one of the female students, Maria Michaelides, finished in the Bacteriology Department and worked for some years at Washington University, although she gave up before achieving tenure. The third student, I believe, quit. I think I was the only one who survived the experience to continue in a career in science.

Dr. Munson was very supportive of my career. When it came time for my thesis defense, someone from the Anatomy Department completely attacked my work. The topic was the neuronal control of adrenocorticotrophic hormone (ACTH) secretion from the anterior pituitary. I had established an *in vivo* bioassay whereby one could detect a corticotropin-releasing factor (CRF) that acted on the anterior pituitary to stimulate ACTH secretion. It was secreted by nerve cells into the hypophyseal portal circulation, illustrating the neuroendocrine pathway.

It turned out that it was not just ACTH secretion that was controlled, but it was all of the anterior pituitary hormones that were under neural control through this neurovascular–neuroendocrine pathway. The basic hypothesis was there, but no one had as yet isolated the so-called releasing factors that were responsible for the pathway from the neuron to the anterior pituitary. My thesis did not carry the project very far, but it established an *in vivo* assay that would be useful for the purification of the releasing factor for ACTH.

I do not know what the Anatomy Professor did not like about my doctoral thesis. It just seemed like graduate students were fair game to be attacked at their final thesis presentations. On my part I was terrified and still suffer mild terror when it is time for my students' defenses.

Dr. Munson had to muster all the support he could get to prevent me from being judged a failure. It was terrifying to see how vindictive a faculty member could be toward a student. In recent years, safeguards have been put in place to avoid such situations.

I do remember that there were two professors in the Physiology Department who took me out to lunch before my qualifying exams and tried to convince me to quit graduate school. They said it was not a place for women. They believed that I would probably just get married, and that training me would be a big waste of funds.

Meanwhile, I was still waiting for my fiancé to be discharged from the service. I waited a year-and-a-half before ending the relationship. What ultimately got to me was when he came back from Alaska, he went to visit his parents before he came to Boston. I was irate and figured it was indicative of something. He was a psychiatrist and I thought, "Do I really matter or don't I?" I decided to break off the engagement, which was a relief considering the difference in our political philosophies.

I had also met Cavin Leeman, another medical student, while at Harvard. He was also going into Psychiatry. He proposed, and I do not fully understand why I accepted. My former fiancé had not really wanted me to work on a career of my own, but with Cavin it was sort of O.K. By this time, I was 27 years old; and I thought it was about time I got married and had a family because that was what I really wanted to do.

So we married, and after a while Cavin did not want me to work anymore. I did not know how to handle that because I did not think I could just stay home and raise children. I thought I would drive them crazy. I have too much energy, and I did not think I had a rich enough inner life to fill the day without having something more serious to think about.

Our conflict over my working was a real hardship, and over time, it turned out Cavin had more antiwomen sentiments than I had originally thought. I remember arguing with him about whether they should increase the enrollment of women at the medical school. Harvard was one of the holdouts. The whole women's movement had to overcome them before they increased the number of women in the medical school class to 50%.

Cavin had finished medical school at that time, and then he interned at the Massachusetts General Hospital (MGH). Interns were paid \$300 per year, and that was not enough to live on. I had just finished my degree, and it seemed like I should have a job.

Dr. Munson came to my rescue then. I was offered a one-year position at Harvard Medical School as an instructor in the Physiology Department. I taught all of the animal experiments. They offered me \$3,000 per year to teach, and Dr. Munson increased that stipend to \$4,500. But the Chair of the department made it very clear to me that I should in no way consider myself to be on the academic ladder. I was just there to be a fill-in.

What I wanted to do anyway was continue working on the CRF problem. I wanted to try to use my own bioassay to see if I could detect the presence of a CRF. I did not know if I could purify it, as I was not a biochemist; but I was game to give it a try.

I only had the job at Harvard for a year, and then it was Dr. Munson who heard about a new program at Brandeis. His wife had been offered a job in the Biochemistry Department there, and they had recently gotten a neurochemistry training grant. He thought that I would qualify, so I went to Brandeis and they took me into the lab to start on the purification of a CRF.

In those early days, I was balancing early career and family life, which included care of my dysfunctional mother. The whole mix was nearly overwhelming at times.

The first time I knew that I was going to have a baby, I went to the chair at Brandeis and said I had to quit. He would not let me. He told me I would never come back if I quit, and he was willing to arrange it with me so that I would not have to work full-time. Three years later, I went back to speak with him again—this time, I was going to have twins. But we continued; and

the chair sanctioned my getting a Career Development Award where I got paid two-thirds time. This was enormously helpful, and something I believe should be done more often. The NIH has never had part-time fellowships for women or men.

When she was a baby, I would take my daughter Eve with me to Brandeis, which had a nursery school. They talk about providing day care facilities to women workers now, and I was lucky to have had that through Brandeis. Eve would go while I worked, and then I would pick her up there and take her to a local babysitter's house. I picked her up there at about 2 or 3 PM.

Then with the twins, I hired a woman, Fanny, to be in the home with them when they were babies. When they were old enough for nursery school, I took them with me to Brandeis. I would pick them up and take them home to Fanny and the au pair girls living in the house, and those arrangements mostly worked out. There was anxiety, but the fact that Fanny was there was an enormous help. When she cut down to 3 days a week, I just managed.

I tried not to talk about juggling family and work too much because there seemed to be this unspoken rule that if you got your work done and accomplished what you were going to accomplish, then no one would bother you. If you asked people for permission, then you could forget about it. It was not going to happen.

Substance P

At Brandeis, the Chair of the Biochemistry Department allowed me to have a graduate student named Richard Hammerschlag. Richard had transferred into the department from MIT and had been floundering around. When I asked him to join the corticotropin releasing factor (CRF) project, he was excited to accept.

We collected hypothalami from a local Boston slaughterhouse, the New England Dressed Meat and Wool Company; but only a few at a time were available. Using these hypothalamic extracts, we established to our satisfaction that a CRF activity could be detected by our bioassay.

With Dr. Nathan Kaplan's encouragement, we decided to scale up because CRF was present in such low amounts. I went to slaughterhouses in Chicago to show the workers where the hypothalamus was located and how to do the collecting. They sent back bags of hypothalami to our lab. We started working with about 2,000 hypothalami. I do not know how I got into working with all of that sludge. I imagine that my mother had wanted me to wear laces.

Our plan was to first attempt purification of CRF on Sephadex columns that would separate CRF from other constituents of the extract by size and then by charge. Then we would devise whatever additional steps were necessary for the final purification. For detecting the biological activity of CRF, we anesthetized rats without stressing them and injected samples of extract

into rats via the tail vein. We would kill the animals 15 minutes later, collect the trunk blood after decapitation, and measure circulating levels of adrenal steroids to see whether the extract could stimulate an ACTH secretion. This was before radioimmunoassay of ACTH.

The division of labor was such that Richard would make the extracts, start the initial purification steps, and I would do the biological testing. We monitored eluates of Sephadex columns by following the $O.D._{280}$. Earlier studies (Guillemin and Shalley) had shown that releasing factors were likely to be peptides and $O.D._{280}$ would be a rough indication of the presence of peptides. Because I had no allegiance to the meaning of $O.D._{280}$, I insisted that we test for CRF activity across the entire column instead of just testing the peaks of the $O.D._{280}$.

One day, when testing some of the eluates from a Sephadex G75 column, I noticed, after intravenous injection of material pooled from a trough of the $O.D._{280}$ activity, that fluid welled up in the mouths of the test animals. I was very surprised and wondered what was happening. I thought the fluid must be saliva, but I was not sure. I was also amused because I had done my doctoral research work in Dr. Munson's laboratory, which was located at the Harvard Dental School, and I thought that perhaps I should know something about secretions of the oral cavity. I remember also racing upstairs from the animal quarters to find Dr. Morris Soodak, a true friend in the Biochemistry Department, to show him this discovery.

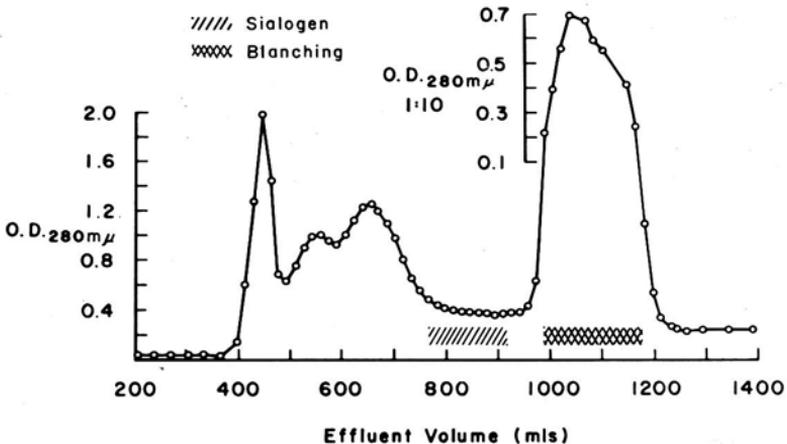


Fig. 1 Gel filtration on a column of G-75 Sephadex of bovine hypothalamic extract: 1.9g was applied in 60 ml of column buffer to a 4.7×69 cm column run in 0.1 M pyridine acetate, pH 2.8, at room temperature; 16-ml fractions were collected at a rate of 60 ml/hour. The region of effluent volume from which sialogogic activity was recovered and the region containing material that caused cutaneous blanching in the test rats are indicated. From Leeman and Hammerschlag (1967).

Shortly afterwards, I collected the fluid with a pipette and bulb and decided to measure the activity of a constituent of saliva, alpha amylase. The results were clearly positive. The sialogogic activity was running on the first purification column as if it were larger than either acetylcholine or catecholamines, and so I suspected it was not a classical neurotransmitter.

The next step was to test whether this activity could be destroyed by proteolytic digestion. We set up a bioassay based just on measuring the volume of saliva. Increasing the dose of extract injected increased the volume of saliva that could be collected simply using a pipette and bulb. We subjected our active fractions to broad-spectrum proteolytic digestion and found that the biological activity was completely destroyed.

I was so relieved because by this time because there were two huge groups, Guillemin and Shalley, purifying the releasing factors, and I did not think I could compete. I thought I had found something different, and I decided to go after it instead. I changed the direction of our entire project. We were now no longer going after CRF, but rather a peptide that could stimulate the secretion of saliva.

That was the industrial part of the preparation. By the time we had finished we extracted over 70 kilograms of bovine hypothalami. Once we had lyophilized the extract, we solubilized the material on the trays and ran the initial purification columns—approximately 20 liters of Sephadex—at Tufts' New England Enzyme Center. We had outgrown the Biochemistry Department at Brandeis and moved to find large-scale homogenizers and lyophilizers. The New England Enzyme Center was set up by the National Institutes of Health (NIH) for people exactly like me, who were working in a classical biochemistry department, but who needed a huge increase in the capacity to extract biological tissue. That facility later became what is now a huge company, Genzyme Corporation.

We brought trays of rats into downtown Boston to test which fractions had the sialogogic activity we were trying to isolate. We then pooled these fractions, took them back to the Biochemistry Department at Brandeis, and continued on with our next purification steps.

We published the first paper just on the detection of "sialogen." Then, when Richard graduated from Brandeis, I had a new student in the Biochemistry Department named Michael Chang. It took 3 more years for Michael and I to isolate the peptide that was causing this secretion of saliva. It was only when it became time for Michael to write his thesis that we began reading the literature on hypothalamic peptides seriously, and we came upon a study about the discovery of something called "substance P."

Substance P had been found in the 1930s by von Euler and Gaddum. In 1931, they were looking at the tissue distribution of acetylcholine and discovered something in horse brain and intestine that caused the contraction of various isolated smooth muscles. Unlike acetylcholine, whose activity could be inhibited by atropine, this new activity was not inhibited.

In 1934, Gaddum and Schild realized that they were dealing with a peptide because it was destroyed by proteolytic digestion. Von Euler and his collaborators ended up naming this peptide “substance P” because it was the substance in the preparations that had this constellation of biological activities: contraction of various smooth muscles, and lowering of blood pressure.

They were unable to isolate the peptide, however, and this became an unfinished project. In their most highly purified preparations, they did have a partial amino acid composition, but they could not decide if there were two amino acids or one.

At Brandeis, we had our pure material and looked to see if it had the biological activities described by Von Euler et al. We did not have rat blood pressure equipment so I went back to the Physiology Department at Harvard asking to borrow theirs. I injected our material into the rats, waiting to see if it would lower their blood pressure, and sure enough, it did.

There was no way out. Our material had the various properties attributed to substance P. We had unintentionally isolated this peptide that had defied isolation for 40 years. We published in the *Journal of Biological Chemistry* in 1970.

One day soon after, I met Von Euler. He was attending a fancy neuroscience meeting at MIT. I had not been invited, but I thought that he might be interested in our story. This was, after all, the peptide that he discovered during his first postdoctoral fellowship in England after getting his degree at the Karolinska Institutet in Stockholm.

Von Euler was aware of our work on the isolation of substance P, and he immediately agreed to meet with me at Harvard Medical School. I told him I could pick him up at his hotel, and we ended up sitting in the parking lot as he asked me for the whole story of our discovery. Meanwhile, the Neurobiology Department at Harvard was wondering where we were, and who was detaining him. It was very nice to talk to him about our work. He really was a gentleman, and very complimentary.

Later he organized a symposium in Stockholm on substance P, and I was invited to come. I went with my husband and three children, and it was an exhilarating affair.

Neurotensin

It was during the course of purification of substance P that I made my second important discovery at Brandeis. This was a vasoactive peptide that we detected in the eluate of an ion-exchange column that was clearly separable from the sialogogic activity. I showed this activity to a graduate student, Robert Carraway, in the Biochemistry Department who happened to be looking for a thesis project. I asked whether he would consider trying to isolate the peptide using this vasoactive assay. He agreed. The complete purification

of this peptide took several more years. We named it “neurotensin” because of its presence in neural tissue and its impact on blood pressure.

Neurotensin has a very broad distribution throughout the CNS, the gastrointestinal tract, the immune system, and so on. Research on neurotensin has become a rather large field. Dr. Carraway has remained on the faculty at University of Massachusetts (UMass) Medical School and continues to be a leader in this area.

At this time, my Career Development Award was coming to an end. I approached the Chair of the Biochemistry Department at Brandeis to discuss my future there and asked whether he was going to recommend me for tenure. He told me that I could stay as long as I wanted and as long as I could bring in my own funding, but that he, for one, would vote against me if asked. He said he would be willing to discuss it with the Department, but he was pretty certain they would all vote against me too. Much to my self-disappointment, the tears began to run down my face. I decided it was time to leave.

Many years later, I was told by a member of the Department that a meeting of the faculty was held to consider my promotion, and that the sentiment of the faculty was in favor of my staying.

But I had made up my mind and was beginning to look for a place to relocate. At the Federation of American Societies of Experimental Biology

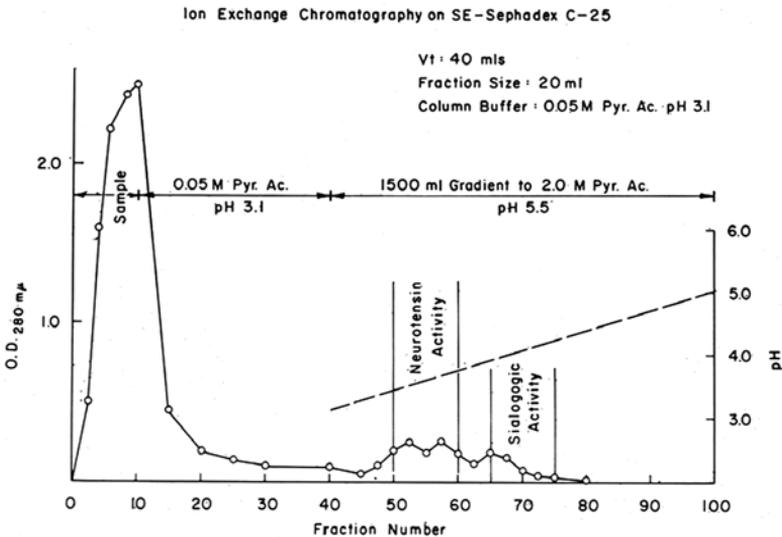


Fig. 2 Ion-exchange chromatography of a bovine hypothalamic extract on sulfoethyl Sephadex C-25. Neurotensin activity (cutaneous vasodilatation) and substance P (sialogogic activity) were detected using bioassays and protein concentration was monitored at 280 mμ. Pyr. Ac. = pyridine acetate. From Carraway and Leeman (1973).

(FASEB) meetings, where Dr. Robert Carraway presented the isolation of neurotensin, I saw John Pappenheimer, a Professor of Physiology at Harvard. He asked me how things were going, and when I said, "Well, not so wonderful," he asked whether I would be interested in joining a new institution at Harvard Medical School, the Laboratory of Human Reproduction and Reproductive Biology (LHRRB). I agreed to look into the matter and made an appointment with Dr. Roy Greep, head of the LHRRB, to interview for a position. My laboratory would be in the Physiology Department.

In 1972, I moved my laboratory to the LHRRB and continued working on both of these peptides, substance P and neurotensin. After I had been at Harvard for some time, a committee headed by Alice Huang began investigating the low salaries of women at Harvard Medical School. As a result of her efforts, I was given raises and was presumably on the academic ladder. The question of being promoted to associate professor with tenure at Harvard was still unaddressed. This mattered very much to me then, and it began to take a toll on my self-respect.

Toward the end of my time at Harvard, Dr. Joseph Martin became the chair of the Neurology Department at MGH. He asked me whether I would move from the LHRRB to his department at MGH, and he said he would support me for a tenured position, feeling that this would not be a problem.

Because my tenure at the medical school was not being supported by the chair of the Physiology Department, I somewhat hesitantly agreed. I gave notice to Dr. Kenneth Ryan, then head of the LHRRB.

I distinctly remember reporting for work at MGH in September, right after Labor Day, only to be told by Dr. Martin that things would not be as he had promised, and that a tenure appointment for me would be much more difficult than he suspected. I was, needless to say, horrified.

After a short deliberation, I decided to ask Dr. Ryan if I could remain at the LHRRB, and, to my relief, he was very welcoming. Still, the question of tenure was haunting me. Now, thank heaven, I don't care about such things.

While still trying to recover from this last experience, Dr. Maurice Goodman, a friend of mine, and a former graduate student in the Physiology Department at Harvard, offered me a position as full professor with tenure in UMass Medical School's Physiology Department, where he was chair. It had the disadvantage of being nearly an hour's drive from my home in Newton, but nonetheless I accepted.

By this time, my older daughter, Eve, was an undergraduate at Harvard, and my two younger children were in high school. I felt concerned about the long commute and being so far from home. But, on the positive side, it seemed like UMass was a much friendlier institution than Harvard, and with less pressure. Many excellent scientists were working on the biology, molecular biology, and pharmacology of the two peptides that my laboratory had isolated, and I still felt like working. I was elected into the National Academy. My salary was raised, and work was going well.

I was asked to consider several different positions as chair; and I most seriously considered going to Mt. Sinai Medical School in New York. I gave up this idea when my husband said that maybe I should consider going by myself. His comment shocked me as I felt that maintaining the family was important. Our marriage was having difficulty, especially around the issue of my professional success compared to his academic career, but I hadn't fully realized how much we had grown apart. During that year, our marriage ended.

Soon after, I was fortunate enough to meet Dr. Lippman Geronimus, an infectious disease expert at Harvard Medical School. He had a wonderful sense of humor, and I admired him for raising three wonderful daughters on his own after death of his wife. Six years into our relationship, he died suddenly at my son's graduation from Oberlin. It took me a long time to get over his death.

These many personal traumas have taken a toll, I believe, in reducing my energy to cope with all the strains of continuing a career in science.

Continuing a Career in Science

I never moved from Newton to Worcester. When David Farb was hired as the chair of Pharmacology at Boston University (BU) Medical School, and he asked me to consider coming to work for him as a professor in his department, it was as much a transportation issue as it was a career move. I had been getting extremely tired on my way home from work, and I wanted to be more available to my family. Of course, by this time, most of my children had been through college and were not around all that much, but I had a feeling of distance. I looked forward to the idea of working closer to Boston.

I had known David as a graduate student at Brandeis and later as a postdoctoral fellow Harvard Medical School. We had even collaborated on a project together.

In 1992, I moved to BU, bringing several people with me. At that time, I was working with Dr. Norman Boyd on the photolabeling of the substance P receptor, and in defining its binding site and other biological functions. Dr. Mark Alexander and I were working on the role of neurotensin in the hypothalamus to stimulate the secretion of the luteinizing hormone-releasing hormone (LHRH). This was a project that I had started with Dr. Craig Ferris when I was still at the LHRRB.

Working at BU has been a difficult but fruitful time. Because I am essentially a team player, I have trouble holding opinions that are in conflict with the administration of the place I work in. There is one thing that BU is doing now that I do not agree with, however. They are building a BSL4 Bioterrorism Research Laboratory without really having obtained permission to open it because the land does not belong to BU. In many of the public hearings on this topic, BU has not treated the community with dignity. This has not helped community relations for the medical school.

One of the really enjoyable experiences at the school has been to super-vice the Ph.D. training of graduate students. Morris Tansky, in particular, has been—with a few rocky times—a real pleasure.

Interactions with other faculty members have been very productive. The involvement of the pharmaceutical industry in the production of antagonists both substance P and neurotensin has opened up new fields of investigation for the possible clinical usefulness of halting the activities of these two peptides. In recent years, I have worked with Drs. Harry Pothoulakis, Arthur Stucchi, and James Becker on anti-inflammatory diseases of the gastrointestinal tract, and with Drs. Stucchi, Becker, and Karen Reed on the ability of substance P antagonists to inhibit cell adhesion formation after surgery in the peritoneal cavity.

Over the years, despite considerable recognition, I sometimes have felt disappointed in myself for not taking on bigger administrative jobs, such as Department Chair. There are many advantages to those types of positions; and there has been pressure for women being offered these opportunities to not refuse because they were not available to them for so long. I have found, however, that I am more interested in ideas, research, and mentoring. To me, the best part of my job is the science—not empire building.

Lately, I find myself getting less and less excited about the general work atmosphere of the biomedical establishment in this country. As time has passed, it has become increasingly difficult to obtain grant funds. I have continued working as a professor and tried to be content making those contributions.

Most recently, I have wanted to think more about how basic neuroscience might contribute to psychiatry. I began working with my daughter, Eve, who is a psychiatrist, on how to think about this link with psychiatric matters—not so much cognitive, but more emotional—that is, thoughts, feelings, anxieties. Although her father is a psychiatrist, I credit her interest in psychiatry as coming as much from me as from him.

I wanted to explore whether there might be any particular insights that would come because of my interest in basic neuroscience. That is when I started thinking about the importance of relationships amongst neurons—with influences from other cells too—on development and function.

It turns out that huge excesses of neurons are born in the nervous system during embryogenesis. Most die off, and only those that establish functional relationships with other cells survive. I thought it was very startling that survival depends, not only on development, but also on function at the cellular level. It seemed to me that this fits as a metaphor for emotional properties.

I asked my daughter if she would think neuronally with me, and she said, “Mom, how else would I think?!”

“OK,” I said, “You’re plenty smart for me.”

I have had a very good time working with her and we published a paper called “Neuronal Metaphors—Probing Neurobiology for Psychodynamic

Meaning,” which met with no notice whatsoever. We sought to apply the functional properties of neurons in their microscopic relationship-networks to the macroscopic world of human emotional properties. We felt that an understanding of neurons at the cellular level as they form and break relationships could inform the psychotherapeutic process in a way that an isolated understanding of receptor chemistry cannot. These neuronal metaphors can powerfully influence the way psychiatrists approach their work in the clinical setting.

I think this is such an interesting idea that I would like to pursue it further. We are planning to present a panel at a psychiatric meeting where we would invite two basic scientists to show the real importance of relationships to the development of neuronal function. Then Eve would give some clinical examples, and we would invite another psychiatrist to also review some patients’ progress in psychotherapy. Finally, we would include a philosopher to elucidate the importance of metaphorical thinking in the advance of scientific understanding.

I do get excited about the possibility, although, at the moment, biological psychiatry has swung so far the other way that I do not know how our ideas will be received. Everyone talks about specific transmitters, and these drugs have been useful, but there is also a need for more psychodynamic thinking.

Life as a Working Grandmother

Family remains a priority in my life these days, and I try to stay connected to my children and grandchildren as much as possible. My oldest daughter, Eve, and her husband, Alberto, have three children, Elena, Claudia, and Alejo. Alberto, a Columbian citizen, works in international affairs with a company that has many dealings with South America.

My son Raphael works nearby in downtown Boston at the investment firm Eaton-Vance. His wife, Dana, is on the faculty at Simmons School of Social Work and has a busy homemaker career life also. They have two children, Marissa and Gabriel. I play ping-pong with them and, occasionally, tennis.

My younger daughter, Jenny, is a completely lovely and accomplished person. She and her husband, Hector, a Peruvian photojournalist, live in Washington, D.C. Jenny is a Professor of Linguistics at George Mason University and is admired in her department as an excellent teacher and a researcher.

These days, my friend, Nelson and I spend summers at our house in Maine, right near Bowdoin College. During the academic year, I have been trying to host more social events—like an afternoon of music in the garage—instead of worrying about work all the time. Nelson and I stay active playing hard-fought games of ping-pong.

I have seen a lot in the news recently about the changing role of grandmothers, and it really is a new phenomenon. We are a generation of older working women, now less available to babysit and participate in family care. Grandmothers today are better off financially than in generations past, and they are looking for better lifestyles for themselves in travel and entertainment. When their daughters and sons have children, they may be busily involved with their own careers and social lives, and less available to help out. This is getting national recognition.

Because I like to make myself available to my family, I find that life as a working grandmother can get complicated. This conflict is just one more that I did not entirely anticipate.

On balance, although it has been fraught with difficulties, my life as a scientist has been very rewarding. It has really been a pleasure to work with graduate students, and to watch them mature into critical, capable investigators. I have found that really fun. As a consequence of having been elected into the National Academy, I have met persons who have asked me to help in editing their manuscripts. That has been a very positive experience as well.

Either as a result of my schooling in elitist male institutions or my own personal problems, I never felt safe to fully commit myself to a career in science. Perhaps things have changed with the greater participation of women at high positions in academia and in the political arena, but that sense of security at work has always eluded me. In this current climate of reduced support for small individual research projects at the NIH, I see signs of the old anxiety now not limited to women, but also applicable to men. I feel a great sadness about this situation.

It seems to me that these changes at the NIH have occurred with the increase in business attitudes toward education, and “bottom-line” thinking. I have observed the continued rise of large sums of money invested at the top to fewer and fewer directors of laboratories, and less and less trickle down to the support of creativity at junior levels. In this hard turf, it is difficult for an old socialist like me to flourish.

I know that I should think about retiring some day, but I am not quite ready.

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