## **Brain Medicine**

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## VIEWPOINT

# Personal recollections of Seymour "Si" Reichlin, MD, PhD: A maven, a mentor, and a mensch

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In this personal tribute, Leonard P. Kapcala, M.D., a former Endocrine Fellow who trained with Seymour "Si" Reichlin, M.D., Ph.D. for 4 years at Tufts New England Medical Center (TNEMC), recounts his experiences and interactions with Dr. Reichlin spanning nearly five decades. These recollections begin with his pursuit of an Endocrine Fellowship, continue through his training years, and extend to his ongoing relationship with Dr. Reichlin up through the celebration of Si's 100th birthday in June 2024 and, most recently, as of January 2025. After training with Dr. Reichlin, Dr. Kapcala went on to a distinguished career in academic medicine, research, biotechnology, and regulatory science. Through intimate vignettes and personal stories, Dr. Kapcala portrays Dr. Reichlin as a scientific maven with unparalleled expertise in neuroendocrinology, a dedicated mentor who provided invaluable guidance and a genuine mensch whose kindness and humanity touched all those around him. This tribute offers a unique window into the remarkable character and profound influence of one of the most distinguished figures in the field of neuroendocrinology.

#### Introduction

This article focuses primarily on my personal recollections of Seymour "Si" Reichlin, M.D., Ph.D., shaped through various interactions over approximately 48 years. My account contrasts with an accompanying publication by Lechan and Toni (1), which comprehensively reviewed Si's life, career, scientific contributions, achievements, and honors in neuroendocrinology, neuropsychiatry, and psychosomatic medicine. While that work documented Si's invaluable contributions to our understanding of the interactions among the nervous, endocrine, and immune systems, I aim to share this remarkable man's personal impact on my life and career.

After training with Dr. Reichlin, I joined the Case Western Reserve University School of Medicine faculty as an Assistant Professor of Medicine in the Endocrine Division. Then, I became a tenured Associate Professor of Medicine and Physiology at the University of Maryland School of Medicine. My basic science research career, which was funded by many federal grants, began with studying the regulation of pro-opiomelanocortin (POMC)-related peptides in the brain and evolved into studying the regulation of brain interleukin-1 by immune stimuli and alcohol. Subsequently, I worked in the biotechnology/pharmaceutical industry at Genetic Therapy Inc. (a wholly owned subsidiary of Novartis) as the North American Clinical Coordinator of the first phase three gene therapy trial (treating patients with primary glioblastoma with the thymidine kinase gene) conducted under the auspices of the U.S. Food and Drug Administration (FDA). I then worked as a Senior Medical Officer in the Neuropharmacology and Neurology Divisions of the Center for Drug Evaluation and Research (CDER) at the FDA, where I primarily worked on the development, approval, and oversight of various neurological drugs (predominantly for Parkinson's disease) and was also a leader in scientific education at the

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Figure 1. Mary Ann Kapcala (Len's wife, left), Len Kapcala (right), and De Sey mour Reichlin (center) photographed at Si's 90th Birthday Celebration at the Chicago Pier in Chicago, Illinois, in June 2014. Mary Ann and Len Enjeyed see ing Si again and celebrating his birthday along with Si's many for mer fellows ird-party yon and friends. ut ermissio

FDA. While at the University of Maryland School of Medicine the Baltimore-Washington Stress Society, which I co-directed with George Chrousos, M.D., Sc.D., Chief of Pediatric Endocrinology, National mstitute of Health and Human Development, National Institutes of Health (Nth) and I also founded the "Maryland Endocrine Group," which I co-difected with Paul Ladenson, M.D., Chief of Endocrinology at Johns Hopkins School of Medicine. trom from these falls

#### My Path to Dr. Si Reichlin at Tufts New England Medical **Center (TNEMC)**

My path to neuroendocrinology/endocrinology began with what fer ike an epiphany during my freshman physiology class at the University of Pittsburgh School of Medicine. Dr. Ernst Knobil (Chairman 🕁 f 🗃 hysiza ogy) captivated me with a lecture about how the hypothal mass begundling the strength of the s livered via the hypothalamo-hypophysial portal system. Learning how this elegant system controlled so many vital organ functions through anterior pituitary hormones (adrenocorticotropic hormone-A 🛱 🗒 growth hormone-GH, thyroid stimulating hormone-TSH, luteinizing hormone-EHa follicle-stimulating hormone-FSH, prolactin-PRL) ignited my passion for becoming a neuroendocrinologist.

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**Figure 2.** Dr. Seymour Reichlin photographed with some of his former fellows at Si's 90th Birthday Celebration at the Chicago Pier in Chicago, Illigo in June 2014. The photograph shows Ron Lechan, Jeff Tatro, Si, Len Kapcala, Rich Robbins, and Bob Gagel from left to right. ithout wa permission

This passion persisted throughout my internal medicine training at Case Western Reserve University Medical Center, where, as a medical resident, I wrote a clinical protocol investigating the kinetics of ACTH suppression from exogenous glucocorticoid treatment. As I approached the completion of my residency, I set my sights on training in neuroendocrinoloav.

Familiar with the Williams Textbook of Endocrinology, I knew that the chapter on neuroendocrinology had been authored by Dr. Seymour Reichlin, who had just completed his term as President of the Endocrine Society. It was clear that Dr. Reichlin was considered one of the foremost neuroendocrinologists in the United States, if not globally. My primary goal was to secure a fellowship at Tufts New England Medical Center (TNEMC) with Dr. Reichlin.

I arrived at my interview with Dr. Reichlin with considerable nervousness but was immediately struck by how this intellectual giant made me feel comfortable. Not only did he thoroughly address all my questions about the fellowship, but he also impressed me with his warmth and genuine interest. I also learned that his scientific prowess had earned him the directorship of the General Clinical Research Study Center at TNEMC. I was also impressed by everyone I met, particularly the Endocrine faculty and several Clinical Fellows.

After deferring acceptances from other prominent endocrine programs to which I had also applied, I received that life-changing phone call from Dr. Reichlin offering me a fellowship position-a moment I still vividly remember. I would begin my journey with him in July 1977.

#### My Experience with Dr. Si Reichlin at TNEMC (1977–1981)

I began my neuroendocrine/endocrine training in the Division  $\vec{m}$   $\vec{m}$ docrinology at TNEMC with Dr. Reichlin in July 1977 and was the only new z clinical fellow for that academic year. At that time, there were four clinical fellow for that academic year. ical fellows, Drs. William "Bill" Cobb, Ira Spiler, Claudio Urosa and Bruce Biller, who had preceded me and who I had met previously at my hterview and who were starting their second year. My arrival in the Digiston was marked by warmth and welcome from everyone—Dr. Reicking the endocrine faculty (Drs. Mark Molitch and Ivor Jackson), the cline and in the second seco search fellows, the laboratory personnel who conducted most endocrine testing for TNEMC, and the administrative staff. During my second clinical year, I was joined by five new clinical fellows: Drs. Ronald "Rond echan David "Dave" MacLean, Richard "Rich" Robbins, Richard "Dick Good man and Alan Moses. Throughout my tenure in the Division, I enjoyed working and interacting with all the fellows and everyone in our Division over the next few years, as it felt like a close-knit family.

Dr. Reichlin was most accommodating when I met with him to decide on a research project/focus. He let me select a basic science  $\vec{e}$  are  $\vec{e}$  (ie g studying adrenocorticotropic hormone—ACTH in the brain) of an great to a studying adrenocorticotropic hormone me. This was an area in which no one else in the Division was engaged in research and would turn out to be my own project with guidance from Dr. Reichlin, with whom I met periodically to review my work and receive advice. Studying ACTH in the brain continued as one active area of basic research throughout my academic career, and subsequently, I added β-endorphin to this focus. Although I had come to TNEMC with an interest

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**Figure 3.** Dr. Seymour Reichlin photographed as he views his birthday cake and is about to blow out the candles at his 100th Birthday Celebration at Maggiano's restaurant in Boston, Massachusetts, in June 2024. This unique birthday cake, made by Dr. Ron Lechan, depicts the human anatomical region (hypothalamus, pituitary stalk, hypothalamic-pituitary portal system, anterior pituitary, posterior pituitary) toward which Dr. Seymour Reichlin devoted much of his life toward studying and about which he was renowned globally as a foremost expert about the neuroendocrinology of this region.

in ACTH relative to the hypothalamic-pituitary-adrenal axis, my research interest became directed toward a different organ, the brain, rather than the anterior pituitary.

My interest in brain ACTH had been particularly stimulated by the recent report by Krieger and co-workers earlier in 1977 (2) that several molecular forms of immunoassayable ACTH (which was also bioassayable) existed in the rat brain and that immunoreactive (IR)-ACTH was highest in the hypothalamus but was also measurable in other extra-hypothalamic sites. Most importantly, this report indicated that IR-ACTH did not appear to have been derived from the anterior pituitary but had originated within the brain. These findings supported findings reported many years earlier by Guillemin and colleagues (3) that the ACTH activity seen in brain extracts arose from a neural source. The interest in brain ACTH would ultimately be related to discovering the functional role(s) of ACTH in the brain, a question that still persists.

One of the first recommendations by Dr. Reichlin was for me to try to develop my own ACTH antibodies for radioimmunoassay (RIA). I followed



**Figure 4.** Len Kapcala (left) and Dr. Seymour Reichlin (right) protographe of the section at his 100th Birthday Celebration at Maggiano's restaurant in Boston, Mask work cannot be such as always admired.

his advice and set about this task by conjugating synthetic ACTH2-24 that carrier protein and then immunizing rabbits. Weeks after the boots free distributed been immunized, they were bled, and serum was collected. I the man RIA to be synthetic ACTH1-39 with lodine-125 and tested the serum in a RIA to be see whether ACTH antibodies had been generated. When the samples with tained at the end of the RIA were being counted, I peeked at the minute results and was so excited to see that a noteworthy specific minute present! Dr. Reichlin's guidance led me to successfully generate several ACTH antibodies that would be helpful throughout my research and be subsequently, I also obtained other ACTH antibodies (West misparity of the antibody supplied by the NIAMDD Hormone Distribution Program of the National Pituitary Agency and C-terminal antibody from Dr. John Keindall and a  $\beta$ -endorphin antibody from Dr. George Chrousos) to boot research.

Dr. Reichlin also recommended that I become involved with a not he potential project available in the Division. Dr. Maurice Raben at THEMG had access to a human pituitary brain bank because he had been solating and purifying growth hormone that had been used to treat children with growth disorders. Soon after I came to TNEMC, Dr. Raben died. However researchers in his laboratory had been working on isolating B-liporropine (LPH) from the pituitaries in the bank. This project appealed to me be a cause there had been speculation that  $\beta$ -LPH might have some relation as ship(s) with ACTH. Dr. Reichlin and I started working with Dr. Rapers  $\beta$ searchers to isolate  $\beta$ -LPH as a purified extract. Eventually,  $\overline{W}e \cong h \partial u g h \overline{g}$ that we had a reasonable purification of  $\beta$ -LPH, and I used this product to immunize rabbits. We obtained a kind, generous sharing of human  $\beta$ -LPH from Dr. Michel Chretien, and I used this  $\beta$ -LPH to label it with Iodine-125 for an RIA to see whether we had been able to generate  $\beta$ -LPH antibodies. We were happy to see that our purified  $\beta$ -LPH was sufficient for generating  $\beta$ -LPH antibodies with noteworthy specific binding. Around this time, the relationship between ACTH and  $\beta$ -LPH became clarified after it was

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Figure 5. Dr. Seymour Reichlin photographed at his 100th Birthday Celebration at Maggiano's restaurant in Boston, Massachusetts, in June 2024 👾 👸 r 🛱 🛱 fellows and former Endocrine faculty, Seated in the foreground, Si, Mark Molitch (former faculty), Alan Moses, and Rich Robbins. Standing in the back ground are Ron Lechan (former fellow and faculty), Len Kapcala, and David MacLean. эe atutory re ģ Ise cove mate

suggested that both ACTH and  $\beta\text{-LPH}$  and related peptides are derived from the same precursor, POMC (4), and this suggestion was confirmed by molecular cloning work (5) a few years later. My work in this area was subsequently integrated with my later research on  $\beta$ -endorphin in the brain when it was recognized that  $\beta$ -endorphin is a fragment of  $\beta$ -LPH.

In addition to my basic science research projects, I also became involved in several Clinical Research projects, with the general aim of assessing ACTH effects on the brain and studying abnormal prolactin secretion. I wrote the protocols for these projects in conjunction with Dr. Mark Molitch, my Endocrine faculty mentor and advisor for clinical research.

Dr. Reichlin would serve as an attending for endocrine consults by our Division a few times a year. When Dr. Reichlin attended the Endocrine Consult service in the hospital, I soon learned that his knowledge of general clinical endocrinology and general internal medicine was also quite extensive, as was his knowledge of neuroendocrinology. It was a special treat when Si would attend on the monthly Consult service. Related to the Consult service, Si held a meeting with the fellows typically once a week, during which one or more cases from the Consult service would be presented to the group and reviewed and discussed. Occasionally, this meeting would focus on a specific clinical or research topic. What was fascinating in these meetings was how Si would often propose some novel hypothesis about some endocrine or neuroendocrine relationship(s), which might seem surprising. However, after one thought about it, his hypothesis might really seem like it had merit and potentially could be true. During these meetings on the Endocrine consult service, Si also often dropped "pearls" about some scientific facts of possibly notable significance that were not well or widely known.

During my second year as a Clinical Fellow, I decided that I wanted to stay longer as an Endocrine Research Fellow. I discussed my desire with Si, and he was supportive of my staying beyond the traditional 2 years of training. He suggested that I also seek NIH funding for this additional research time in the Division. Si also informed me of potential Veteran Administration (VA) funding to support my Research tenure and helped me write my first NIH grant application. This application was subsequently successfully funded and provided me with financial support for my additional research time at TNEMC.

On a more personal level, Si's door was always open to any me to come? and talk with him (within the constraints of his busy office and traveling schedules) about anything. He could be a good "Father Confessor" for any issue or concern. I remember one time when faced with a personally challenging and depressing experience/problem, I met with Si and he was very supportive and encouraging. He made me feel much better and encouraging. problem. Si took a real interest in people in his Division and would occord casionally inquire about the status of my newly acquired hobby in Boston running marathons. He also gave good career advice and was most neurophic to me when I was planning to leave the Division and take my first academic faculty position.

Attesting to Si's caretaking nature for his Division, he and  $\overline{H}$  is wife Ellie, would host a summer picnic at their house every year. This pic nic was an event people in the Division looked forward to every year. Si's bene polent shepherding of his Division was mutually reflected by how people in the Division thought and felt about Si. I cannot recall ever hearing any one speak ill of Si and suggest that Si was respected and beloved throughout the Division (including Endocrine faculty, clinical and research fellows Endocrine laboratory staff, and administrative staff) and TNEM@Clinical Research Unit for which Si was the Director.

Looking back on those 4 years from 1977 to 1981 in Boston (two as a Clinical Fellow and two as a Research Fellow), I cherish the warmest memories of professional growth and personal connection. What began as a professional relationship with Dr. Reichlin would evolve into a life-3 long mentorship and friendship that has profoundly shaped my  $c_{a}$  eer alife—a journey I am privileged to share in the following pages.

### My Lifelong Connection with Dr. Si Reichlin Beyond TNEMC

After leaving TNEMC, I kept in touch with Si periodically up to the present time. Most of my contact with Si was when we ran into each other at a

scientific meeting, most commonly the Annual meetings for the Endocrine Society and the Society for Neuroscience. Occasionally, I would speak with Si on the phone. I remember calling Si to share my joy and inform him that I received my first NIH grant after leaving TNEMC as a faculty member at Case Western Reserve University School of Medicine. Not surprisingly, Si congratulated me and seemed proud.

Many years later, I invited Si to take time from his busy schedule to come for a 2-day visit as a Visiting Professor at the University of Maryland School of Medicine. During this visit, Si gave a Medical Grand Rounds and a research lecture and met with scientific faculty, especially neuroendocrinologists. We also had a nice dinner and had a lot of great conversations about various subjects. I was very proud of my mentor, who graciously agreed to visit my workplace.

Two experiences with Si strongly attest to his generosity and relationship with me, and to his willingness to apply his exceptional knowledge, expertise, and experience as well as his desire to help one of his former fellows. Not only is he famous, but importantly to me, he is also a considerate, kindhearted, and nice person. First, I was contacted by Si when he informed me that the ACTH antibodies that I had generated during my fellowship training at TNEMC had been commercialized. He further noted that he wanted to send me several thousand dollars from this commercial transaction. I told him I was surprised to hear about this and was most grateful for his thinking about me and his plan to share some money. Upon receipt of this money, I diverted it to my basic science laboratory research program. The second experience relates to a recent discovery of a letter I had saved that reminded me of Si's generosity. This was a 12-page, singlespaced letter that had been typed. It was Si's detailed review of an NIH grant application I had sent to Si, and I asked him for feedback before submitting it to the NIH. Si's letter provided incredibly detailed feedback on the whole grant application. For example, he cited a specific part of the grant, such as page three, paragraph four, as a reference to his comment, and then he gave detailed comments about that section. The whole letter of feedback followed this paradigm and provided me with positive and constructive negative feedback on the grant. When I received this in the mail, I was so pleased to have Si's feedback and found it to be extremely helpful. He had devoted countless hours to reviewing my grant application in such great detail and then providing detailed, written feedback because I believe that he thought that detailed written feedback would be more helpful and useful to me than discussing the grant over the phone. His efforts had far exceeded what I was hoping for and what I had expected, but nevertheless, his detailed review was tremendously appreciated!

In 2014, I learned that Si's former fellows were planning to get together at the Annual Endocrine Society meeting in Chicago to celebrate Si's 90th birthday. When I learned of this, without any question, I immediately planned to attend, as did my wife, Mary Ann, who knew Si and wanted to attend. We attended this celebration and enjoyed seeing Si again, as well as many former fellows we had not seen for some time (see Figures 1 and 2). It was a very nice celebration. Si looked great, and we had pictures taken with him. We had a chance to catch up on our lives.

My next opportunity to see Si was recently in June 2024 when we learned that plans were being made to celebrate Si's 100th birthday in Boston because the Annual Endocrine Society meeting was being held in Boston. Again, upon learning of this event, my wife and I planned to attend. It was great to see Si again, as well as many former fellows and other staff from TNEMC (see Figures 3–5). We had a chance to speak with Si and get pictures. Si looked great and not much different from when we had seen him at his 90th birthday celebration 10 years earlier!

Before seeing Si at this 100th birthday celebration in Boston, I had the pleasure of speaking with Si on the phone for over an hour but was cautious about not letting Si know that I would see him shortly at his upcoming celebration in Boston. My stimulation to call Si was to offer my condolences on the recent loss of Si's 98-year-old "baby" brother (as Si had referred to him), Herbert, whose death in April 2024 had been noted in a Washington Post obituary describing Herbert's august career and his relatives, including Si. Si informed me that he was about to travel to the memorial service in Raleigh, N.C., for his "baby" brother and then to Boston for the Endocrine Society Annual Meeting. We caught up with each



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other's lives and discussed various topics. Although it was amazing, I was not surprised to hear that Si, at 100 years of age, was writing two books, one on the neuroendocrinology and neuroimmunology of Alzheimer's disease and another on the neurobiological basis of ecstatic mysticism. One subject we discussed was Si's recall that I play the accordion and his me minding me of how I had played my accordion at one of his annuals upmer Endocrine Division picnics, which he and Ellie, Si's wife, hosted in Weston at their farm/home. Although I had noted that I no longer play the बेटला क्र dion frequently, Si encouraged me to play more frequently. I had for gotter about my playing at the picnic, but it was amazing that Si recal ted my play ing nearly 50 years earlier! Although we had not spoken so extensively for many years, we had not lost a step in maintaining a close relationship othe ights stipu

#### **Concluding Remarks**

My accounts of various interactions with Dr. Si Reichlin over 48 years reflect my recollections of those experiences and provide insights into my thoughts and feelings about Si. Although it is impossible to depice a person in one or a few words, one can try to describe a person with some descriptive words despite this impossible task. Consequently with provide a few words that give insight into this most remarkable person  $\overline{z}$ se oDerivat Dr. Si Reichlin. e exce g/lice 9 Pub

Given this approach, I believe that Dr. Si Reichlin is:

- 1. A maven, because of his exceptional knowledge and expertise
- 2. A wonderful mentor, given my personal experience of to w file has interacted with me, helped me, what he has meant to me, and also that his many fellows have a similar view of his mentoring, and  $\overline{\triangleleft} \ \overline{o}$
- 3. A mensch, considering his personal qualities as an extraordinary person.

The term "maven" can be described as "someone who is dazalingly skilled in any field. Synonyms: ace, adept, champion, genius, motshoto mavin, sensation, star, superhero, superstar, virtuoso, whiz, wizz wizz wizard." These words aptly depict Si relative to his expertise in  $\overline{e}$ docrinology.

One description of a mentor I found is as follows: a "collaborative learning relationship that proceeds through purposeful stages over time and has the primary goal of helping a mentee to acquire the essentia competencies needed for success in a research career." Another descore tion is: "Mentoring is a reciprocal learning relationship which admende tor and mentee agree to a partnership, where they work collaboratively toward the achievement of mutually defined goals that will develop  $a_{\perp}^2$ mentee's skills, abilities, knowledge, and/or thinking." I agree with either of these descriptions that Si has been a great mentor for me. ŧ

Finally, a mensch can be described as "a person who is honorable, kind and thoughtful and is someone to admire and emulate. The term is used as a high compliment, implying the rarity and value of that individual's qualities." Without any question, these words clearly describe the won a derful and nice person that Si is.

I view Si as one of the few most influential and impactful people in my life, and I hope that what I have written will help convergentiate a real markable, wonderful, and nice person he is. My wife, Mary Ann, and look forward to celebrating Si's 110th birthday in 2034! der tec ē

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Currently retired; main former affiliations?

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