



The Life and Times of Dr. Robert Sherwin, One of the Greatest of Great Diabetes Investigators

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I did not know Dr. Sherwin until 1975, when I began my fellowship in endocrinology at Yale University. However, I later learned of Bob's lovely family, which consisted of his mother (Frieda Sherwin) and father (Harold Sherwin) as well as his very accomplished brother, Dr. Paul Sherwin (an English professor at City College in New York City). Bob had many outstanding accomplishments as a trainee prior to his time at Yale. Perhaps his greatest accomplishment was as a star on his high school baseball team, which won the city championship in Yankee Stadium. As he is a Yankees fan, I have no doubt that this was Bob's most outstanding early achievement. As an undergraduate student at Union College, Bob not only received honors in biology but he also met his future wife, Leslie, who played a key role in his future successes, especially their three children, Ben, Sara, and Jenny. As a born-and-bred New Yorker, Bob received his MD degree at Albert Einstein College and completed his residency in medicine at Mt. Sinai Hospital on the Upper East Side of Manhattan. Prior to coming to Yale as a postdoctoral fellow, Bob worked under Dr. Reubin Andres at the National Institutes of Health (NIH), where he modeled insulin kinetics using the previously unheard-of insulin clamp technique. He joined the Yale faculty as an assistant professor in 1974 and retired 44 years later in December of 2018.



Robert Sherwin as Director of Endocrinology at Yale University, New Haven, CT.

Bob Sherwin's Early Mentoring Career

When I started as a pediatric endocrine fellow at Yale in 1975, the period of training was limited to only 2 years (the first year primarily clinical and the second year primarily research). I was fortunate to be selected for my second year of research training in diabetes with Dr. Sherwin, who was a young assistant professor in the Department of Internal Medicine. I will never forget my first meeting with Bob, who suggested I work on some of his experiments with "trained" dogs. I quickly found out how truly challenging it was to carry out experiments with dogs (they were not really trained and I always came home smelling like a mangy dog). Consequently, I was really glad when Bob asked me to switch to a new set of studies in humans, as humans smelled better and you did not have to feed them.

At that time, there was a hot debate between diabetes investigators at the University of Texas Southwestern (i.e., Drs. Roger Unger and a young Philip Raskin) and investigators at Yale (i.e., Drs. Philip Felig and Robert Sherwin). The Texas group contended that diabetes was a bihormonal disease, i.e., not enough insulin and too much glucagon, whereas the Yale group contended that insulin deficiency alone was the main cause of diabetes. The Texas group seemed to have won this debate when somatostatin became available through the pioneering work at the Salk Institute in California. In the Texas study, a bolus of somatostatin injected into healthy, normal control subjects lowered both plasma insulin and glucagon levels. Surprising to the Yale group was that the dose of somatostatin used by the Texas group resulted in a fall in plasma glucose levels. If insulin was so important, plasma glucose levels should have increased, not decreased, following a shot of somatostatin. Dr. Sherwin immediately countered with the suggestion that while there might be acute effects of suppression of plasma glucose, hyperglycemia

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Robert Sherwin during his residency at the Mount Sinai Hospital, New York, New York.

still depended primarily on long-term reductions of plasma insulin. Bob offered me the opportunity to test his hypothesis, which was confirmed by a 6-h infusion of somatostatin in healthy individuals without diabetes. Namely, the long-term suppression of plasma insulin resulted in hyperglycemia and ketosis that was unaffected by exogenous replacement of endogenous glucagon.

Paradoxically, the concept of long-term suppression of glucagon in youth with well-established type 1 diabetes (T1D) resulted in the initial studies of insulin pump therapy at Yale. Specifically, Dr. Sherwin agreed with my suggestion to study 2- to 3-day infusions of somatostatin in youth with T1D. Since such patients were already severely insulin deficient, my hypothesis was that somatostatin might be of some benefit to youth with T1D by chronically lowering plasma glucagon levels. The obvious question was how to infuse exogenous somatostatin for several days. The answer was the auto-syringe pump that was being used to provide long-term, subcutaneous infusions of an iron-chelating agent in youth with iron overload. This pump was being used by the Yale Pediatric Hematology group to provide a stable continuous infusion of desferrioxamine. I did not realize at the time that the pump also had a red button, called the instant dosage button, that could give large bolus doses of the drug being infused. Eureka! Forget about somatostatin—this was a new

way to administer insulin, and it worked.

An important takeaway from our early insulin pump studies was that, even during his early years as an assistant professor, Dr. Sherwin was a terrific mentor who had an impressive reservoir of diabetes knowledge that he shared readily with his young trainees. Many of us could point to the role that Dr. Sherwin played in the development of our own careers, since one of Bob's greatest qualities was to allow his junior colleagues to get full recognition for studies in which they participated.

Take the impact of the Kroc Study, for example (1). This was a multicenter study that included world-renowned diabetes investigators like Drs. Keen, Alberti, and Kohner in the U.K.; Drs. Rizza, Service, Bergenstal, and Rubinstein in the U.S.; and Dr. Dupre in Canada. Dr. Sherwin stood out among this incredible array of talent, which resulted in Yale serving as the data coordinating center of the Kroc Study. Even more important, the results of the Kroc Study set the stage for the Diabetes Control and Complications Trial (DCCT), and it was Dr. Sherwin who stepped aside so that I could serve as the principal investigator for the Yale center in the DCCT. With Dr. Sherwin's assistance, I have remained principal investigator of the Yale center in DCCT/Epidemiology of Diabetes Interventions and Complications (EDIC) since 1983.

Monday Morning Research Meetings

I always think of the golden age of clinical diabetes research at Yale as covering my first 25 years at the Yale School of Medicine, and Bob Sherwin deserves most of the credit. In retrospect, it is clear that our weekly diabetes research meetings always pulled our group together. These meetings were held almost every Monday between 10:00 a.m. and 12:00 p.m. to discuss the progress of current studies as well as suggestions and plans for new projects. They were held in a conference room two floors above Bob's office. One of the highlights of the meetings was a visit by our Lilly representative, who almost always brought coffee, bagels, and other treats to keep us going. It is amazing how much was accomplished during these meetings.



Robert Sherwin, William V. Tamborlane (currently chief of medicine pediatrics, Yale University), and Mike Genel (currently professor emeritus, Yale University) with two of their first insulin pump patients.

Bob always led these meetings, even though he was often late in arriving. His favorite question for all of his colleagues was, "What's the question that we are trying to answer?" However, there was at least one time when his standard question backfired. On that particular occasion, Bob was late in arriving at our Monday meeting, as usual. It was not surprising that he opened with his usual remark, namely, "What's the question?" My quick retort was, "Too late—the study is over; today we are going over the results." Clearly, Dr. Sherwin was not infallible, just infallible most of the time.

The Monday meetings were exciting because we always had terrific fellows and bright trainees from Yale and other U.S. medical schools who kept all of us on our toes, like Mary Rudolf, Susan Boulware, Peter Merkel, and others. We enjoyed the input of Drs. Don Coustan, Al Reece, and Mike Diamond, who led our diabetes in pregnancy studies. We also had a steady stream of top young investigators from Europe and Australia. Dr. Koivisto was the first trainee who came from Finland to work with Dr.

Phillip Felig, the chief of endocrinology in internal medicine. Dr. Koivisto had T1D himself, and, without any prompting from Bob or me, he agreed to be our first outpatient to use an insulin pump. It was not until years later that we discovered that he had gone back to multiple daily insulin injection therapy.

Two of our next stream of international trainees came from Italy to work with Bob, namely, Luigi Sacca and Sonia Caprio. Dr. Sacca served as Bob's right-hand man for the first few years before returning to Italy. Sonia Caprio was unique in that she trained in internal medicine in Italy and worked in Philadelphia while her husband completed his training in engineering, and they both came to New Haven when he received an assistant professor appointment at the Yale School of Engineering. As a result, Sonia showed up one day at Bob's office looking for a job. Bob's first comment to Sonia was, "Unfortunately, we don't have any open positions at the moment." Sonia's response was, "That doesn't matter, I'll work for free." His response was, "OK, it's a deal." What a deal this turned out to be! Not only has Dr. Caprio excelled and remained at Yale all of these years, but she is now professor of pediatric endocrinology and retains a well-oiled research program in obesity and type 2 diabetes in adolescents. Sonia is the first and only self-trained pediatrician in our program.

The next wave of outstanding young investigators came to Yale from the U.K. and Ireland. One of our first U.K. recruits was Dr. Stephanie Amiel, who was completing a stint as a registrar with Dr. Harry Keen in London. I was lucky to meet Dr. Amiel at a diabetes meeting on insulin pumps that was held in Paris. I was not enjoying the Paris meeting very much, especially the first day, since I was the second speaker on the morning schedule. The bad news for me was that Dr. Keen spoke immediately before my presentation, and he covered everything I was going to say. The good news occurred on the second day of the meeting, when Dr. Amiel agreed to come to Yale after completion of her work with Dr. Keen. Although Dr. Keen tried to get Bob to hire one of his other registrars, Dr. Sherwin could not have been more pleased once Dr. Amiel arrived in New Haven.

Over the next 5 or 6 years, Stephanie published more than 10 articles, including three important articles in the *New England Journal of Medicine* and three others in the journal *Diabetes*. Unfortunately for us, Dr. Amiel ultimately decided to return to the U.K. to continue her career. Bob was convinced that she decided to leave Yale because she thought that Americans did not care for her classic English accent. She did not realize that Americans always assumed that the proper use of English indicated that the speaker must be very smart. On the other hand, she may have hoped to meet her future husband, Professor George Alberti, by returning to London.

Drs. David Kerr and David Maggs led the next set of investigators from the U.K. who joined our group. David Kerr ultimately returned to Bournemouth, England, whereas David Maggs took an alternate route by joining a series of pharmaceutical companies in the U.S. In addition, Dr. Margaret Griffin had an endocrine appointment at Yale prior to returning home to Ireland. Although not

from the U.K., Dr. Tim Jones traveled all the way to New Haven from Perth, Australia. He closed the deal to join our group in a way that was very similar to the approach used by Sonia Caprio. Somehow, Jones found my telephone number and called my office to see if there were any openings in the Yale diabetes research program. My first answer was no, until he told me that he already had acquired funds to support his work at Yale from the Australian Sammy Davis Jr. Telethon. My second answer was, "When can you start?" Thank goodness Dr. Sherwin approved of Dr. Jones joining our team. While at Yale, Tim published eight articles (including an important *New England Journal of Medicine* article) prior to returning to Australia and being promoted to chief of pediatric endocrinology at the Princess Margaret Hospital for Children. More recently, the hospital was reopened as the new Perth Children's Hospital. Tim remains as chief of pediatric endocrinology, and his group in Perth has produced many original and interesting articles.

Based on the encouragement of JDRF, Dr. Sherwin was able to recruit both Dr.

Table 1—Advancements and awards received during Dr. Sherwin's career

Year	Advancements and awards
1990–1993	Associate Editor, <i>Diabetes Care</i>
1993	David Rumbough Award, JDRF
2000	President, American Diabetes Association
2000	Director, Center for the Study of Hypoglycemia, supported by a JDRF grant
2001	Banting Medal for Service, American Diabetes Association
2003	Director, Yale General Clinical Research Center, which was subsequently combined with the Pediatric Unit and maintained under new names by the NIH Clinical Translational Science Award Program
2003	Two MERIT awards, NIH
2005	Section Chief of Endocrinology, Department of Internal Medicine, Yale School of Medicine
2005	Director, Yale Center for Clinical Investigation, supported by an NIH Clinical Translational Science Award
2007	Banting Award for Scientific Achievement, American Diabetes Association
2011	Albert Renold Award, American Diabetes Association
Undated	Edward H. Ahrens, Jr. Award for Patient-Oriented Research, Association for Clinical and Translational Science Naomi Berrie Award for Achievement in Diabetes Research, Columbia University Worldwide Lifetime Achievement Award John K. and Mary E. Davidson Award, University of Toronto Distinguished Alumnus Award, Albert Einstein College of Medicine

Prezemyslaw Lapaczewski and his wife, Monica, who were medical school classmates in Poland. When asked how he liked New Haven a couple of weeks after his arrival, Prezemyslaw's surprising remark was that he thought the city was dirty. It was also noteworthy that he and his wife were actually married over the phone: Prezemyslaw in his office at Yale and Monica while still in Poland. Bob kept both of them, and they turned out to be very careful investigators. Not surprisingly, he changed his name to Walter Borg, which is a lot easier to spell than Prezemyslaw Lapaczewski.

Bob Sherwin's Later Career

Times change and, hopefully, we all mature. Bob really turned the corner with his promotion to director of the endocrine training program in the Section of Endocrinology in 1984. Shortly thereafter, Dr. Sherwin was promoted to professor of internal medicine, followed by a move to a much larger office in a new building some distance from his prior one.

Bob's later career was characterized by substantial increases in basic science studies. These included autoimmune

studies with Drs. Janeway and Flavell, basic research in brain glucose-sensing mechanisms, and effects of fructose on brain metabolism and brain processes in type 2 diabetes. Dr. Sherwin was also the director of the National Institute of Diabetes and Digestive and Kidney Diseases-funded Diabetes Center at Yale from 1993 until his retirement in 2018.

Dr. Sherwin's career continued on its upward trajectory throughout his career, characterized by numerous advancements and awards (Table 1).

Sherwin published ~50% of his ~400 publications prior to 1996, and I was a coinvestigator on ~100 of those articles. On the other hand, the remaining 50% of articles were published from 1996 to 2018, and most of these had new young investigators as coauthors. The coauthors included postdoctoral fellows and other colleagues, like Drs. Jacob, Dziura, Barrett, Heptulla, Wen, Solimena, Attia, McCrimmon, Russel, Sinha, Savoye, Evans, Enoksson, Inzucchi, Weiss, Yeckel, McNay, Page, Herzog, Rothman, Constable, Jastreboff, Aguiar, Van Name, Gianini, Santoro, Hwang, and Small, to mention just a few.

Summary

Prior to his retirement, Dr. Sherwin was a member of 18 of the major professional organizations related to diabetes in the U.S. and Europe, the recipient of 22 diabetes honors and awards, and a member of the editorial board of 15 journals as well as a member of numerous national committees. Moreover, Dr. Sherwin was invited to give a near-endless stream of lectures related to diabetes throughout his career. In his last years as section chief, Dr. Sherwin held multiple grants from the NIH and others that totaled millions of dollars of support. It was no accident that it took three established professors to fill only two of Bob's long-standing grants. It is hard to imagine that anyone will have the credentials to fill Bob's shoes in the future. I am just glad to have had the opportunity to work with him.

Reference

1. Champion MC, Keen H, Pickup JC, Tamborlane WV, Dupre J, and the Kroc Collaborative Study Group. Origin and design of the Kroc Collaborative Study. *Diabetes* 1985; 34(Suppl. 3):13–16