Diabetologia (2013) 56:435–438
DOI 10.1007/s00125-013-2833-0

IN MEMORIAM

# George S. Eisenbarth, 1947–2012

**M. A. Atkinson**

Published online: 25 January 2013


*In the end…isn't it all about the dash?*

By convention, nearly every memorial notes three important facets of information: the name, the birth date and the date of death of the deceased. Beyond the obvious benefits and challenges associated with one's name, much of life is spent with annual recognition of an individual's date of birth, begrudgingly or not. At the other end of life's spectrum, the date of a person's death is also often subject to much in the way of recognition, perhaps most notably, the question of 'How long did he or she live?'– as if the primary goal in life involves a quest to see who can live the longest. However, in composing this memorial, I would posit that, while birthdays and the duration of one's life are certainly of value, the most important carving etched into a piece of granite or noted in raised letters on a bronze plaque is one simple element, the '–'. For with this mere and simple singular stroke of punctuation, the purpose of a life, as well as what was accomplished through it, is recognised.

George S. Eisenbarth, born on 17 September 1947, passed away on 13 November 2012, after courageously battling with pancreatic cancer for a year and a half. His '–' is a story well worth sharing, as it reflects a picture of one who overcame barriers, cared for others, demonstrated intellectual persistence and extended a degree of professional unselfishness that should not only inspire many, but serve as an example for others to follow.

George grew up in a working class neighbourhood in Brooklyn, New York. From when he was very young, his parents nurtured a pathway for him to seek a career in science and medicine. Indeed, in a personal conversation a few years back, George shared with me that, in his early life, his mother would read to him from a scientific encyclopaedia; this, while he would row a boat on a lake in one of New York state's mountain ranges. Likewise his father, who worked at the Natural History Museum in New York City, would continually encourage George to visit that facility with the hope that this would spur a curiosity, as well as a career, in science. Yet, interestingly, neither his mother or father had much in the way of formal education; neither completed high school. Somehow, undoubtedly related to the persistence of his parents' efforts, George broke through these economic and familial educational barriers, graduating from New York's Grover Cleveland High School in 1965. Given the limited economic opportunities that characterised his community it is not surprising that only a small percentage of his fellow high

M. A. Atkinson (✉)
Department of Pathology, College of Medicine,
The University of Florida, Gainesville, FL 36210-0275, USA
e-mail: atkinson@ufl.edu

M. A. Atkinson
Department of Pediatrics, College of Medicine,
The University of Florida, Gainesville, FL 36210-0275, USA

school graduates would continue on to college. George, being a part of that minority, went on to attend Columbia University, New York, through an even more rare and prestigious offer, a Pulitzer Scholarship.

After graduating in Biology from Columbia—a possibly unexpected achievement given his background—he continued his educational journey on to Duke University (Durham, NC, USA) where, in 1975, he earned an MD/PhD degree. It was at Duke that George's interest in endocrinology was nourished through the mentorship of Harold Lebovitz, a well-known physician–scientist. As an endocrine fellow with Lebovitz, George oversaw what eventually became a well-recognised study establishing an association between human leucocyte antigens (HLA) and the autoimmune polyendocrine syndrome type II [1]. With this, it was clear that his parents' dream had become a reality. However, the '–' for George's life was far from over.

George left Duke as a young and spirited investigator to work at the National Institutes of Health (NIH) in Washington, DC. There he worked with the Nobel Laureate Marshall W. Nirenberg, a biochemist who, together with Robert W. Holley and Har Gobind Khorana received acclaim 'for their interpretation of the genetic code and its function in protein synthesis'. In Nirenberg's lab, George was involved in the generation of the first monoclonal antibodies directed against islet cell antigens (back then, an innovation in itself), including the A2B5-anti-complex ganglioside. In collaboration with Barton Haynes and Anthony Fauci at NIH, he also generated some of the first anti-T cell monoclonals (anti-CD-7 and the anti-transferrin receptor).

In 1982, the world-renowned Joslin Diabetes Center (Boston, MA, USA) recruited George. Once there, he put innumerable hours into collaborative studies with colleagues on twin pairs either concordant or discordant for type 1 diabetes, as well as on family members of those with the disease. It was through these efforts that he developed 'the figure'. While no known program or publication would allow for verification of the following statement, it would be my contention that no concept in the modern history of type 1 diabetes has been more recognised, plagiarised, conceptualised, questioned or tested than 'the figure', published by *The New England Journal of Medicine* in his 1986 landmark article, 'Type 1 diabetes: a chronic autoimmune disease' [2].

That figure (Fig. 1), based on seminal studies performed by George and taken in concert with the related findings of others, changed the thinking of the entire field regarding the pathogenesis of type 1 diabetes; taking it from a disease widely considered to be of acute onset to one where a long asymptomatic period characterised by silent autoimmune destruction of the insulin-producing pancreatic beta cells occurred. That viewpoint, demonstrated so elegantly, not only put forward the potential whereby a specific intervention might allow for the reversal of type 1 diabetes but, more importantly, it placed into

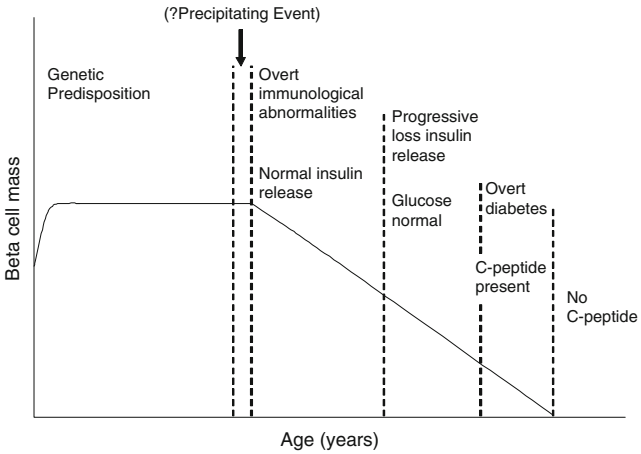


**Fig. 1** The natural history of type 1 diabetes. From [5]

contention the notion that the disease could ultimately be prevented. This concept, a means of preventing type 1 diabetes, became the ultimate '–' for George, in terms of providing a compass for his professional career.

Another noteworthy event during George's time at the Joslin Diabetes Center involved his hiring of a young Japanese researcher named Masakazu Hattori. At that time, the type 1 diabetes research community was exceedingly interested in performing studies on a new animal model of type 1 diabetes, the so-called 'non-obese diabetic' (NOD) mouse. However, access to those animals during this period was extremely limited and largely restricted to the efforts of a small number of investigators in Japan. Through the diplomatic efforts of George (as well as Ed Leiter of the Jackson Laboratory) along with Masakazu, NOD mice eventually became available to investigators worldwide. Indeed, without their efforts, it is unclear as to when that animal model, which eventually became a standard for type 1 diabetes research, would have become available. NOD mice have proven themselves extremely valuable for efforts seeking to identify genes forming disease susceptibility and therapeutic screening of agents, as well as in understanding the role of the immune system in type 1 diabetes development—a massive body of literature that was made possible, in part, through the efforts of George.

While what he achieved during his life up to and through the Joslin Diabetes Center was noteworthy, George's intellectual contributions to this disease were far from over. Indeed, a major part of George's life story occurred after his move from the Joslin Diabetes Center to the Barbara Davis Center for Childhood Diabetes at the University of Colorado in 1992. During his two decades of service as Executive Director of that facility, he worked with his colleagues to build the institution into one of the leading type 1 diabetes centres in the world, from both a research as well as a clinical care perspective.

On his move to Colorado, George carried with him a profound and unbending interest in specific forms of autoantibodies he had previously identified in the blood of non-diabetic twins whose brothers or sisters already had diabetes. His relocation allowed for a marked expansion of efforts exploring the role of type 1 diabetes-associated 'biochemical' autoantibodies in family members of probands with the disease, as well as in the general population. His research over the last two decades also made a vital contribution to efforts allowing for genetic testing of risk of type 1 diabetes (in newborns as well as in adults), developing more accurate means of disease prediction through the use of improved and expanded autoantibody testing methods, the identification of beta cell antigens, characterising the rates of metabolic loss in the period prior to symptomatic onset, and so much more. A large part of his 'plan' for improving disease prediction as a means to prevent the disease was spelled out in a 2001 article that over time has become something of a citation classic [3], having nearly a thousand notations in the medical literature. A generation later, his efforts have allowed for population-based efforts involving the genetic- and autoantibody-based testing of hundreds of thousands of newborns, children and adults to assess their vulnerability to the life-altering disease type 1 diabetes. Put another way, programmes such as the NIH Natural History Study, the Trial to identify the Environmental Determinants of Diabetes in the Young (TEDDY), and the Diabetes Autoimmunity Study in the Young (DAISY) at the Barbara Davis Diabetes Center were, without question, strongly influenced by George's vision and leadership.

Thankfully, his efforts in type 1 diabetes research did not go unnoticed. Indeed, the list of accolades he received throughout his lifetime is composed of the highest national and international honours for those in diabetes, including the ADA's Outstanding Scientific Achievement Award (1986), the Pasteur–Weizmann/Servier Prize in Biomedicine (2006), the ADA's Banting Medal for Scientific Achievement honouring meritorious lifetime career achievement in diabetes research (2009), the Mary Tyler Moore and S. Robert Levine Excellence in Clinical Research Award from the JDRF (2012) and the Albert Renold Award from the ADA (2012).

The Renold award is especially noteworthy for its purpose—mentorship and training—for it is in this area that George's legacy will continue for decades to come. George was an outstanding mentor to more than three generations of diabetes researchers from all parts of the world. His basic teaching to trainees included sheer logic, critical thinking and approaching complex problems through proposition of simple, key questions…free of bias or preconceived ideas. His teaching also included openness and collaboration. Quite strikingly, he openly practised the sharing of ideas and unpublished data with others, even those who could be perceived as competitors—a generosity that was much appreciated in the scientific community. With this, he taught trainees to recognise the value of advancing science through acting unselfishly. George's passion for data, and sharing them with others, was not restricted to trainees. Indeed, he participated in many efforts where discovery was enhanced through collaboration, including, but not limited to, the Diabetes Prevention Trial—Type 1 (DPT-1), JDRF Autoimmunity Prevention Centers, NIH Autoimmunity Centers of Excellence, NIH TrialNet, NIH Immune Tolerance Network, Brehm Coalition and JDRF Network for Pancreatic Organ Donors with Diabetes (nPOD).

Also, while much of the type 1 diabetes research community may consider George as an individual with full-time focus on that disorder (this, given the degree and breadth of his accomplishments in studies of that disease), such a belief would be far from accurate. George was, as hoped for by his parents, a physician–scientist at heart. Because of this, over the years he provided seminal contributions to the knowledge pool for many other disorders, including Addison's disease, autoimmune polyglandular syndromes and coeliac disease. In short, his quest for data combined with scientific curiosity took him to many places.

Any memorial to George would also be remiss if it did not mention his unwavering belief that immune reactivity against the insulin molecule itself represented a driving force in the formation of type 1 diabetes. So strong was his belief in this notion that he once published an article with the shortest of possible titles, 'It's insulin' [4]. George did not advocate this position lightly, only becoming the primary spokesperson for the cause after many years of intense pursuit characterising the immune response against this molecule, in humans as well as in a variety of animal models of type 1 diabetes.

Over these last 2 years, George's most pronounced intellectual passions were directed at two areas, studies of the human pancreas (via nPOD) and understanding the interactions within a trimolecular complex formed by an HLA molecule, antigenic peptide and the T cell receptor. He strongly believed that characterising the pathology of the human pancreas (including the composition of the T cell receptors in the inflammatory lesion), as well as understanding the boundaries by which the trimolecular complex operated, would not only lead to the development of a novel class of drugs capable of preventing type 1 diabetes but, in addition, unlock the mystery of why type 1 diabetes develops.

In each of these aspects, George was long supported by his wife, Frieda, as well as his children, Stephanie and Stephan. George also found much in the way of support from his colleagues at the Barbara Davis Diabetes Center; a remarkable group of individuals to whom he would often redirect credit and celebrity. (George remained, true to his background, humble and did not seek praise for himself).

George also took particular pride in belonging to a group known as the Brehm Coalition, a cooperative of which I too am a part and in which members see a degree of support, friendship and scientific collaboration that is unique in science today. However, throughout his journey with cancer, George found support from the entire type 1 diabetes research and care community. Here, he once again provided a model of tenacity and persistence, attending lab meetings up until mere days before his death. While the disease compromised his ability to speak during his final days, he remained passionate about hearing scientific data from others. Perhaps, just perhaps, this was a purposeful and peaceful experience on his part, designed to take life back to the times with his mother, just listening, in the rowboat, about a half-century ago.

George's life's work was extraordinarily extensive and wide-ranging, with his studies of tens of thousands of research participants, 500 or so publications, hundreds of lectures and dozens of trainees and colleagues. It is my opinion that he purposely sought to orchestrate efforts supporting his strong belief that type 1 diabetes is a disease where prevention is possible. This message will not lose resonance despite his death as, thanks to his efforts, it has travelled throughout the type 1 diabetes research community. Indeed, because of the guidance George provided by 'the figure' and his life-long leadership by remarkable example, I have full confidence that his vision will one day be achieved and his '–' will be seen, through the eyes of history, as being one of remarkable purpose.

## References

1. Eisenbarth G, Wilson P, Ward F, Lebovitz HE (1978) HLA type and occurrence of disease in familial polyglandular failure. N Engl J Med 298:92–94
2. Eisenbarth GS (1986) Type I diabetes mellitus. A chronic autoimmune disease. N Engl J Med 314:1360–1368
3. Atkinson MA, Eisenbarth GS (2001) Type 1 diabetes: new perspectives on disease pathogenesis and treatment. Lancet 358:221–229
4. Wegman DR, Eisenbarth GS (2000) It's insulin. J Autoimmun 15:286–291
5. Eisenbarth GS (1984) Autoimmune beta cell insuffinciency — diabetes mellitus type I. Triangle 23:111–124