

Remembering Daniel Porte, Jr.



This past weekend saw the peaceful passing of Daniel Porte, Jr., at the age of 91, in the comfort of his home and surrounded by family. Dan was a giant in the world of diabetes research and his legacy lives on in our programs at UW.

Born in New York City in 1931, Dan attended medical school at the University of Chicago after graduating from Brown University, then completed his medical residency at UCSF. After beginning his research career focused on cholesterol metabolism, he moved to UW for fellowship training in the Division of Metabolism, Endocrinology and Nutrition in the Department of Medicine, which at that time was led by its first chairman, Robert H. Williams. Upon the discovery of the radioimmunoassay for insulin, Dan switched his focus from lipid metabolism to glucose homeostasis and diabetes research. His research program made a remarkable series of discoveries that are now so fundamental that most of us take them for granted:

- The inhibitory effect of epinephrine on insulin secretion, leading to the larger concept that pancreatic beta-cell function is regulated by input from the autonomic nervous system.
- Beta-cell dysfunction characterized by loss of both glucose sensitivity (and hence of first-phase insulin secretion) and maximal insulin secretion are an early and primary cause of hyperglycemia in type 2 diabetes (at the time, the prevailing dogma was that type 2 diabetes is caused by insulin resistance and “beta cell exhaustion”).
- Sympathetic inhibition of insulin secretion is more pronounced in patients with type 2 diabetes than in normal subjects.
- The amount of insulin secreted in response to a glucose challenge is influenced by a variety of factors extrinsic to the islet, such as obesity and associated insulin resistance.
- Work led by Steven Kahn, while training with Dan, included showing that in humans insulin secretion and insulin sensitivity are coupled to one another in a manner that can be described mathematically as a hyperbolic function. They also demonstrated the critical importance of this relationship when interpreting the beta-cell’s response in health and disease.
- Dan played an instrumental role in the development and clinical translation of the ‘Minimal Model’ method of quantifying determinants of glucose tolerance, developed by Richard Bergman.

- Dan recruited Dan Cook to UW, who was the first to show the role played by ATP-sensitive potassium channels in the mechanism underlying glucose-induced insulin secretion.
- Working with Steve Woods in the Department of Psychology at UW, Dan also developed and tested the hypothesis that circulating insulin is transported into the brain, where it acts as a negative feedback signal involved in energy homeostasis.
- Work led by Mike Schwartz while training with Dan includes the demonstration that insulin crosses the blood-brain barrier via a receptor-mediated transport system, and that it acts in the hypothalamus to inhibit AgRP/NPY neurons.
- Much of this early work on insulin in the brain set the stage for our current understanding the role played by leptin in energy homeostasis and the concept of 'leptin resistance' in obesity.

As a mentor, Dan had the ability to motivate his trainees through a combination of creative brainstorming and 'friendly but tough' criticism. If you could convince Dan of the legitimacy of your findings, you had no concerns about presenting your work to the rest of the world. Trainees were motivated to discover for themselves how things fit together, rather than assuming that published work can be taken as dogma. If your findings are solid, you will eventually be proven right even if your work departs from the status quo -- so stick to your guns, and don't doubt yourself if your work is reproducible.

Dan spent most of his academic career in Seattle as the Associate Chief of Staff for Research at the VA Puget Sound Health Care System. Dan was also the founding Director of the NIDDK-funded Diabetes Research Center at UW, which is now in its 47th year. He also volunteered his time serving as President of the American Diabetes Association in 1983-1984. Finally, he was the recipient of the highest awards given for scientific endeavors in the diabetes field as well as national recognition for his training prowess.

Dan will be missed, but his legacy lives on.

Michael W. Schwartz

Steven E. Kahn