In Memoriam: Henri Begleiter, PhD

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HENRI BEGLEITER WAS an exuberant man. He approached life and science with enthusiasm. He was a true intellectual, happy discussing and debating ideas, and had an encyclopedic knowledge of the literature.

My closest association with Henri was as part of the Collaborative Study on the Genetics of Alcoholism (COGA), and it is from that perspective that I am writing. Henri played a leading role in the conception and organization of COGA and was its principal investigator from the start until his untimely death. In addition to his contributions to understanding the neurophysiological aspects of alcoholism, about which others will write, his role in organizing and leading the COGA project represented a major and lasting contribution to alcohol research and the genetics of psychiatric diseases.

The idea of a large project to identify genes that affect the risk for alcoholism was audacious, at or ahead of the leading edge of science. Henri, Dr. T.-K. Li, and others worked to persuade NIAAA to support the idea and to persuade Congress to appropriate additional funds to NIAAA for a large collaborative genetics project so it would not take funds away from investigator-initiated R01 grants. NIAAA, led by Dr. Enoch Gordis, decided the time was right and solicited proposals. Henri took the lead in organizing a collaborative project with 5 sites in response to the initiative. COGA was reviewed and funded, along with a proposal from Dr. Ray Crowe at the University of Iowa. Henri took the lead in inviting the Iowa group to join COGA as an additional, fully integrated site. COGA was at the time the largest genetics project at NIAAA and probably at NIH.

The group that got together to conceptualize and organize the large genetics project that became COGA included many leading alcohol researchers, experts in many different areas. Each had a unique perspective, and each was used to directing successful research programs, not to being one participant among many. The discussions about how to ascertain the alcohol-dependent probands and how to assess the complex phenotype of alcoholism and its many comorbid conditions were long and heated. Henri led those many discussions and helped shape the consensus. With many different opinions about the best interview instrument to use, the outcome was the design of a new instrument combining the strengths of existing ones; this became the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA; Bucholz et al., 1994; Hesselbrock et al., 1999), which has been adopted by many groups both in the United States and around the world. An important early decision that grew in large part from Henri's pioneering use of electrophysiology to gain insights into brain functions relating to alcohol dependence was an emphasis on endophenotypes as an approach to aid in the identification of genes that affect risk for alcoholism. While the use of endophenotypes is more common now, it was ahead of its time when proposed, and Henri was an ardent champion of the approach.

Low amplitude P3(00) was known from Henri's work to be a trait related to alcoholism and other disorders; it could be detected in children of alcoholics (Begleiter et al., 1984) and was a potentially useful marker of risk. So EEG phenotypes were incorporated into the COGA assessment. To ensure the comparability of data across sites, Henri insisted that all 6 sites use identical amplifiers, caps, and instrumentation, and he oversaw the design, installation, and training (Cohen et al., 1994). This shows Henri's attention to the details that lead to high-quality data.

The planning meetings and later steering committee meetings that Henri chaired grappled with many important issues. Every one of the strong-minded individuals shared the goal of doing the best science possible, but at times arguments could be long and passionate because there were different ideas of how best to proceed. Henri was a strong leader, but one who allowed discussions to continue until consensus emerged. Out of those long and sometimes uncomfortable meetings came decisions (Begleiter et al., 1995) that in retrospect have stood the test of time very well, a tribute to his leadership and to the cooperative spirit of the group.

Henri would often say he was not an expert in molecular genetics. But during the time that the COGA project was being organized, Henri took a 1-week, hands-on molecular biology workshop sponsored by NIAAA, at which I lectured. He wanted to try for himself some of the molecular techniques that might be used. Henri liked to get a personal feel for the details of the science, so he could better appreciate the tasks facing the project. I think that reflected his tremendous enthusiasm for science, and an appreciation that data do not just appear in pristine form.

Henri enjoyed good food and established a tradition of getting together for dinner the evening before COGA

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Steering Committee meetings. Chinese banquets organized by T.-K. Li when the meetings were in Indianapolis were a particular highlight. These dinners helped establish and maintain friendships among the participants and integrate new investigators into the group. The good feelings that came out of the dinners carried over to soften the edges of what could sometimes be contentious meetings the next day.

Henri received many honors for his work, among them the RSA Distinguished Researcher Award (1992) and the RSA Seixas Award For Service (1995), the Mark Keller Award (1999), and the Jellinek Memorial Award in 2000 "For his outstanding use of multidisciplinary approaches to the study of neuroscience and genetic factors in alcoholism."

Henri devoted much time and effort to leading COGA and was proud of its accomplishments. But his eyes really lit up when he was discussing a new mathematical way to analyze electrophysiological data that he thought would open new avenues into understanding the brain. On occasions over the past 5 or 6 years when we privately discussed the future of COGA, he said that he looked forward to stepping down as PI and spending more time in the neurodynamics laboratory, pursuing the neurobiological and mathematical interests that were so close to his heart. Although he did not get time to do that, he leaves a giant legacy of scientific work, both in electrophysiology and in the genetics of alcoholism. Henri also leaves many friends and colleagues who have been inspired by him and will continue the research that was so large a part of his scientific life.

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