

OBITUARY

Theodore Reich, M.D. (1938–2003)

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Theodore Reich passed away on December 25, 2003. He was the Samuel and Mae S. Ludwig Professor of Psychiatry and Professor of Genetics at Washington University School of Medicine, St. Louis. He is generally regarded as one of the founders of modern psychiatric genetics, with a bibliography in that area that extends from 1969 to 2004. He was a founder of the International Society of Psychiatric Genetics (ISPG) (1993), served as president of that group (1993–1996), and received the ISPG Lifetime Achievement Award (1998). He was renowned as an innovator in genetic analysis and was widely respected as a teacher and a mentor, with former students in influential positions in many parts of the world. He was a major force in the development of national collaborative networks to study the genetics of psychiatric disorders, especially in the investigation of alcohol dependence and the affective disorders.

“Ted” was born on October 14, 1938, in Montreal and received bachelor’s and medical degrees from McGill University there. He went to Washington University in 1965, as a resident, and remained there, except for a fellowship at the University of Edinburgh, for the rest of his professional career. He retained his Canadian citizenship and became, with great pride, a naturalized American citizen only during his last decade. At “Wash U,” Ted was chief resident in 1968–1969 and then left for Edinburgh to study with the renowned geneticist D. S. Falconer. Even as a resident, he had begun collaborative relationships that he would maintain for many years, particularly with his mentor George Winokur, a pioneer in systematic family studies of psychiatric disorders. (Winokur, recipient of the ISPG Lifetime Achievement Award in 1993, passed away in 1998). Winokur and Reich, together with Paula Clayton (former Chair at the University of Minnesota), published the highly influential *Manic-Depressive Illness* in 1969, with a substantial section on family studies and genetics, including the first report of X-linked inheritance in that disorder.

At Edinburgh, Reich adapted the multifactorial model of Falconer to complex medical disorders; his adaptation utilized multiple thresholds for semicontinuous traits. Under appropriate conditions, this enhances the discrimination of multifactorial conditions from single-gene con-

ditions by use of family or twin data. After his return to St. Louis to assume a position as assistant professor, he continued this work, publishing, with Robert Cloninger and Samuel Guze, a series of three articles in the *British Journal of Psychiatry* (1975) elaborating the multifactorial model and demonstrating its utility in the study of sociopathy (now called “antisocial personality disorder”) and hysteria (now called “somatization disorder”). He showed the two disorders to be related in families and also concluded that women with sociopathy were more genetically “deviant” than men with sociopathy and had more affected relatives. His collaboration with Cloninger (another ISPG award recipient) would extend over the subsequent 25 years. They, together with John Rice, published a series of three papers on multifactorial inheritance in the *American Journal of Human Genetics* in 1979, together with related papers in *Biometrics* and the *Annals of Human Genetics* in the same year. These papers described a general model of familial resemblance, including cultural and specific familial as well as genetic factors. The model is admirable in its comprehensiveness, if daunting in its complexity.

Ted served as director of the Mental Health Clinical Research Center at Washington University from 1978 to 1986 and as scientific director of the Alcohol Research Center from 1970 to 1992. He also directed a National Institute of Mental Health (NIMH) training grant for many years, focusing on psychiatric genetics. He counts many investigators in clinical psychiatric genetics among the mentees and scholars in residence supported by these programs, including Peter McGuffin, Nick Craddock, Peter Holmans, Paul van Eerdewegh, and David Garver. Scientists from many countries passed through the “Wash U” program, but Ted had a particular affection for India. He served in Nepal as a medical officer with the Thomas Dooley Foundation between 1964 and 1974. While there, he traveled widely throughout India. He married his wife, Wendy, in a Jewish ceremony in Bombay during the time of his medical duties. In later years, he visited India on multiple occasions and began clinical collaborations in psychiatric genetics with Indian scientists, identifying this as an opportunity for exploration of genetic factors in a different and largely unstudied cultural setting. Collaborators from India (most recently, S. Ghosh, who developed a new nonparametric analytic method) have

benefited from the opportunity to work in residence with Ted and his colleagues.

Ted participated in several historic collaborative projects that have defined the course of psychiatric illness, validated diagnostic criteria, and, more recently, explored the genetics of these disorders in a systematic way. The multisite Collaborative Depression Project began in the early 1980s and continues to this day; among the contributions of the project were the confirmation of sex differences in the prevalence of depression, the description of a substantial birth-cohort effect, and the exploration of the significance and limitations of the family-history method in clinical psychiatry. In the late 1980s, the alcohol-research community became aware of the opportunity and need for a large-scale study of genetic effects in clinical alcohol dependence. The Collaborative Study of the Genetics of Alcoholism (supported by the National Institute on Alcohol Abuse and Alcoholism) was organized, substantially through the efforts of Henri Begleiter, Ted Reich, and T. K. Li. Ted became national co-principal investigator of the project. His energy and wide knowledge of study design led the group to include the development of a new interview instrument (the Semistructured Assessment of the Genetics of Alcoholism [SSAGA]) and a policy of systematic ascertainment of alcohol-dependent subjects. Multiplex families were then selected for intensive study (including DNA endophenotypic measures, such as evoked potentials). A genomic survey was completed, and, in the past several years, specific single genes appear to have been identified, with confirmatory studies from other groups. Ted also led the collaborative group to the next logical step (and one of his key interests): the identification of young people at high genetic risk for alcohol-related disorders and the initiation of follow-up studies. His work on bipolar illness, as part of the NIMH Genetics Initiative, followed a similar path.

It would be fair to say that Ted was known most widely among his scientific colleagues as a speaker and theoretician. He was full of ideas, and he shared them without hesitation, formally or informally. He was an inspiration to students but, more than that, a teacher to

his colleagues. He had an unusual combination of dominance and approachability, never shrinking from an argument, always believing in the rectitude of his position, but not cutting off discussion prematurely or using his position to prevent debate. He was never happier than when confronting an unsolved intellectual problem. When in doubt, he would return to the data and produce illuminating analyses, which might lead to a vociferous defense of a new position. When in the minority, he would rarely concede defeat, but he would accept group consensus and move on to the next point of contention. The collaborative process would often be exhausting but never dull and never personally hostile. It was a set of memorable dramas, with Ted always a central figure.

Ted was bonded indelibly to Wendy and his children, Johnathan and Sarah. He was immensely proud and caring of them. His granddaughter, Sophie, was born in early December 2003, during Ted's final battle with cancer, and this news lifted his spirits substantially. In an irony of fate, he lost his voice for much of the last several years and communicated largely with the use of a handheld board and marker. This was still effective, and there were numerous occasions on which scientific decisions were made by a relay of the scrawl from Ted's board. Despite his long illness, he never lost the need for intimate involvement in the scientific quest and the hunger for new findings. He will be appropriately honored by an enduring award for new investigators from the ISPG. He leaves >200 papers in the scientific literature, with a number still in press; they include seminal contributions to the genetics of complex disease and applications that clearly define specific psychiatric disorders as part of the medical canon. He led the field of psychiatric genetics from relative chaos to a point of equality with the status of many other complex disorders, in which some specific genes are identified and confirmed, and the confirmation of others may reasonably be expected. He will be remembered as a giant in this field, for his personal qualities as well as his scientific contributions. To those of us fortunate enough to have been his colleagues, he will be a legend.