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OBITUARY

Obituary: William L. Nyhan, MD, PhD. (1926–2026)

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Bill Nyhan was one of the most influential people in Biochemical Genetics for decades. Born March 13, 1926, in Boston, Massachusetts, he attended Harvard University (A.B., 1945), Columbia University (M.D. 1949), University of Illinois (Ph.D. 1958), Yale University (internship and residency, 1949–1955). His first focus was on amino acids in cancer when he joined Johns Hopkins University as an Assistant Professor in 1955. However, while working with Barton Childs studying amino acids in the first described case of propionic acidemia, he entered the field of inborn errors of metabolism. Then in 1964, with his student, Michael Lesch, he discovered the remarkable phenotype associated with hyperuricemia now known as the eponymous Lesch–Nyhan syndrome. He joined the faculty at the University of Miami in 1966 and then moved to La Jolla as the founding Chair of Pediatrics at the University of California San Diego in 1969, at the age of 44. He brought a number of talented people with him, including Nadia Sakati and Larry Sweetman, who built the laboratory and kept it running for many years. As a young man in a new department, he cultivated an atmosphere of enthusiasm and attracted a very talented faculty. it was also popular to come to La Jolla to collaborate, and several individuals visited, later becoming leaders in the field worldwide, including Claude Bachmann, Kuniaki Narisawa, Magdelena Ugarte, Cornelis Jakobs, Georg Hoffmann and Jean-Marie Saudubray. There was also a long list of trainees and fellows who went on to distinguished careers, including Stephen Kahler, Mike Gibson, Ted Page, Jon Wolff, Sylvia Estrada, Deborah Marsden, Bob Naviaux, Fred Levine and Bruce Barshop. A host of other talented people also came to work beside him through the years.

There have been many seminal discoveries in the laboratory over the years. The disease known as 3-methylcrotonylglycinuria was found to actually be a multiple carboxylase deficiency due to a defect in holocarboxylase synthetase. A deficiency of 3-methylglutaconyl-CoA hydratase was found in a subset of patients with 3-methylglutaconic aciduria. Some of the first methods were developed for diagnosis in amniotic fluid. The defect in mevalonic aciduria was found to be mevalonic acid kinase, the first defect to be discovered in the pathway of cholesterol biosynthesis. A deficiency of succinic semialdehyde dehydrogenase was found in 4-hydroxybutyric aciduria. A long collaboration with Jean-Marie Saudubray centered on clinical metabolism, leading to a scheme for management and a nosology of metabolic disease.

At the same time, he was an active presence across town on the hospital side. He was a master diagnostician, with a keen clinical eye. Bill retired as Chair in 1986 but continued to oversee the Biochemical Genetics laboratory and clinic activity. It was surprising to see him begin to slow down around the year 2020.

William Nyhan died on February 11, 2026, 30 days shy of his 100th birthday. He is survived by his son, Christopher Nyhan; daughter-in-law, Montine Jannette Nyhan, three grandchildren, and three great-grandchildren. He was a remarkable man. He had a natural grace, which translated from his famous tennis game to his professional life. He was very supportive of his trainees and generous in sharing credit. He was authoritative but not authoritarian, proud but not haughty, epicurean but also ascetic,

a man of letters but of few words. He was an inspiration, and he influenced a generation of investigators and clinicians.

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