BIOGRAPHICAL MEMOIRS

Maria Iandolo New

December 11, 1928–July 26, 2024
Elected to the NAS, 1996

A Biographical Memoir by Bert O'Malley and Mone Zaidi

On July 26, 2024, we sadly lost a giant in academic medicine, Maria Iandolo New, one of our most revered and distinguished pediatrician-scientists of modern times. Maria passed away at her home in Manhattan at the age of ninety-five after a prolonged illness. In addition to being an icon of scientific and clinical brilliance—the first chair of any medical school department in New York City and among very few women chairs in the country at the time—Maria was regarded as powerful, resilient and, at times, intimidating, but with unfathomable compassion towards her colleagues, friends, and importantly, her patients.

Maria Iandolo was born on December 11, 1928, in Brooklyn in a home birth to a closely knit Italian family that deeply valued music. Although others in her family did not go to college, her parents recognized Maria's brilliance from an early age and encouraged her to study. After attending an honors program at Julia Richman High School in Manhattan, Maria managed to get into Cornell University in 1946, at a time when admitted students were overwhelmingly veterans joining through the G.I. Bill. One such veteran was Bertrand New, who had been an officer in the U.S. Navy, but the war ended before he saw combat. The two met in a romantic way, with Maria having trouble swimming in a swift current in Fall Creek on the Cornell campus and Bertrand, the volunteer lifeguard on duty, rescuing her. Both applied to medical school, and Maria, a great student, received a rejection from an upstate medical school stating that she was "an impudent young woman" to presume to take the place of a man who would contribute something to medicine, whereas she, as a married woman, would contribute nothing. The University of Pennsylvania took a chance on both of them, and they were the first married couple to attend medical school together.

Maria earned an M.D. from the University of Pennsylvania in 1954 and following her internship in medicine and residency in pediatrics at New York Hospital, she completed two National Institutes of Health (NIH) research fellowships under Ralph Peterson, focusing first on biochemistry and renal function, and later, on the study of hormone synthesis from the adrenals and gonads during childhood. In 1964, she was appointed chief of pediatric endocrinology at the Cornell University College of Medicine, a position she held for

forty years. In 1978, she was named Harold and Percy Uris Professor of Pediatric Endocrinology and in 1980 was appointed chair of the Department of Pediatrics at Cornell and pediatrician-in-chief at New York Hospital. Her distinguished tenure as department chair lasted for twenty-two years, during which she also founded and directed the eight-bed Children's Clinical Research Center, one of the nation's most prolific pediatrics clinical research centers, which conducted groundbreaking research in endocrinology, hematology, and immunology, particularly during the AIDS epidemic. In 2004, New was recruited to the Mount Sinai School of Medicine as a professor of pediatrics and human genetics and director of the Adrenal Steroid Disorders Program, a position that she retained until her retirement in 2020.

Maria's career exemplifies the link between clinical and basic science, with the constant goal of benefiting patients. Her remarkable clinical discoveries have their roots in her relentless investigation of the course of disease in an individual patient. Yet, she remained in the vanguard of science, pioneering the use of molecular genetic diagnosis and prenatal diagnosis and treatment. Specifically, her creative study of an unusually large group of patients with congenital adrenal hyperplasia (CAH)—whose trust was essential to learning about the extremely private symptoms of their illness and to maintaining regular clinic visits over some forty years—is unparalleled in pediatric medicine. Maria thus presents a model in bioscience of care of the individual and daring inquiry using all the resources of evolving technologies. The strong focus and broad canvas of her life's work show the rich rewards of humanitarian medical research.

Although steroid physiology was well understood when Maria began her scientific career, little of the knowledge had been applied to the understanding of steroid disorders in children. Her seminal research on the mechanism and genetics of steroid disorders established standards for pre- and post-natal care for patients with CAH. In 1979, Maria described a form of mild steroid 21-hydroxylase deficiency (which she termed "nonclassical"), as the most frequent of all autosomal recessive disorders, predominantly affecting Eastern European Jews.[1] A spectrum of severity of CAH had always been noted, but Maria was first to identify the mild form with specific molecular genetic mutations. More recently, with the help of cutting-edge molecular dynamics in collaboration with Shozeb Haider from University College London, she was able to identify specific structural changes in CYP21 as predictors of disease severity.[2] Over almost forty years, Maria followed more than 250 patients with nonclassical 21-hydroxylase deficiency, obtaining extensive family histories, and genetic, hormonal, and clinical information. She published a detailed genotype-phenotypic correlation study of 1,507 CAH patients in 2013.[3] Maria's achievements also include establishing aldosterone deficiency as a cause of salt-wasting CAH; delineating the hormonal norms for classical and nonclassical CAH; and discovering new *CYP21A2* mutations causing CAH.

Maria pioneered prenatal diagnosis and treatment of CAH. Using her unique treatment protocol, which was challenged occasionally by the naysayers, Maria remained a powerful proponent of the efficacy and safety of prenatal dexamethasone for affected female fetuses. In addition to being safe for both mother and child, this protocol also avoided reconstructive genital surgery and potential psychological damage to both the child and family. Together with Dennis Lo of Chinese University of Hong Kong, Maria was able to diagnose CAH by quantifying cell-free fetal DNA in maternal plasma as early as six weeks of gestation, thus making it possible to provide immediate and effective prevention of genital ambiguity.[4]

In 1977, Maria first described a new syndrome, apparent mineralocorticoid excess (AME) in a Zuni girl.[5] AME is an autosomal recessive disorder with prominent clinical manifestations, including low birth weight, polyuria, failure to thrive, severe hypertension, hypokalemia, and low serum aldosterone and plasma renin activity. Her team was the first to publish mutations on the 11b-HSD2 gene causing this form of low renin hypertension. In discovering and studying AME, Maria also opened a new field of receptor biology. She showed that the 11b-hydroxysteroid dehydrogenase type 2 enzyme (11BHSD2) acts at the mineralocorticoid receptor of the distal renal tubule to metabolize cortisol to cortisone, and thus protect the receptor.

Maria held the longest continuously funded NIH grant, for forty-three years, that supported her studies on the diverse clinical spectra of patients with rare steroidogenic enzyme defects. In 2003, she was awarded a new grant from the NIH's Office of Rare Diseases through which she created a consortium that included medical centers in New York, Texas, Brazil, and France and became an integral component of the then-new NIH Roadmap for Medical Research.

Maria's deep commitment to training physician-scientists stemmed from her thirty-year experience as director of the premier Accreditation Council for Graduate Medical Education-accredited Pediatric Endocrine Training Program at Cornell. During this time, she trained nearly every future chief of pediatric endocrinology in New York City, and more than 100 pediatric endocrine fellows, most of whom have gone on to become leaders in academia and industry. Up to two years before her death, Maria had a thriving clinical practice, and her laboratory of molecular genetics, licensed by New York State for twenty-five years, received samples from all over the world for diagnosis of adrenal disorders, as well as other endocrinopathies. Among her many extra-institutional

contributions, Maria served as president of the U.S. Endocrine Society as well as the Lawson Wilkins Pediatric Endocrine Society. She served as editor–in–chief of the *Journal of Clinical Endocrinology and Metabolism* for more than six years and edited an authoritative textbook, *Genetic Steroid Disorders*.

In all, Maria New's work has improved and advanced the world of pediatric endocrinology in a way rarely achieved in the past century. In recognition of her many accomplishments, she received numerous honors, including the Endocrine Society's highest honor, the Koch Medal, as well as the Robert H. Williams Distinguished Leadership Award; the Rhone-Poulenc Rorer Clinical Investigator Award; University of Pennsylvania's Distinguished Graduate Award; and the 1996 Dale Medal, the highest award offered by the British Endocrine Society. In 2003, Maria New was inducted into the National Institute of Child Health and Human Development's Hall of Honor. In 2006, she was awarded the Allan Munck Prize conferred by Dartmouth Medical School, recognizing "an individual deemed to personify Allan Munck's excitement for science, dedication to teaching, impeccable intellectual honesty, collegiality, and thoughtful mentoring." In 2007, New, an Italian-American, was elected to the Italian Endocrine Society, and in 2010, won the Judson J. Van Wyk Award of the Lawson Wilkins Pediatric Society, and the Ceppellini Award from the European Federation for Immunogenetics. Maria New was an elected member of the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences. In 2022, Mount Sinai launched an award to memorialize Maria's legacy, the Maria I. New International Prize for Biomedical Research, which is endowed through the generosity of one of her many dear friends, economic historian and Pulitzer Prize-winning author Dan Yergin and his wife, foreign policy expert, Angela Stent.

Not only was she a towering figure in academic pediatrics, Maria was also an executive force for her family, particularly after the death of her husband. She leaves behind three children, Erica, Daniel, and Antonia, who became physicians, their spouses Alan Lerner, Kim New, and Ben Zipursky, eight grandchildren, and four great-grandchildren.

Acknowledgments

The authors are grateful to Maria's daughter, Antonia New, M.D., vice chair for Education at the Department of Psychiatry at Mount Sinai, for providing details of Maria's early life.

References

1 New, M. I., et al. 1979. "Acquired" adrenal hyperplasia with 21-hydroxylase deficiency is not the same genetic disorders as congenital adrenal hyperplasia. *J. Clin. Endocrinol. Metab.* 48:356–359.

2 Haider, S. et al. 2013. Structure-phenotype correlations of human CYP21A2 mutations in congenital adrenal hyperplasia. *Proc. Natl. Acad. Sci. U.S.A.* 110:2605–2610.

3 New, M. I., et al. 2013. Genotype-phenotype correlation in 1,507 families with congenital adrenal hyperplasia owing to 21-hydroxylase deficiency. *Proc. Natl. Acad. Sci. U.S.A.* 110:2611–2616.

4 New, M. I., et al. 2014. Noninvasive prenatal diagnosis of congenital adrenal hyperplasia using cell-free fetal DNA in maternal plasma. *J. Clin. Endocrinol. Metab.* 99:E1022–1030.

5 New, M. I., et al. 1977. Evidence for an unidentified steroid in a child with apparent mineralocorticoid hypertension. *J. Clin. Endocrinol. Metab.* 44:924–933.