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In Memoriam

Sumner J. Yaffe: The Father of Pediatric Clinical Pharmacology

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INDEX TERMS clinical pharmacology, memorial, pediatric, Yaffe

ABBREVIATIONS CRMC, Center for Research for Mothers and Children; IOM, Institute of Medicine; NICHD, National Institute of Child Health and Human Development; NIH, National Institutes of Health; PPRU, Pediatric Pharmacology Research Units

J Pediatr Pharmacol Ther 2011;16(3):162–166

On August 10, 2011, the pediatric community lost one of its most eminent pioneers and staunchest advocates with the death of Sumner J. Yaffe, MD (Figure 1). He was 88 years of age. It was through his tireless efforts and unwavering commitment to pediatric pharmacology, his research creativity, his exemplary leadership, and his warm and gentle humanity that Sumner J. Yaffe changed the face of therapeutics in neonates, infants, and children, worldwide.

Sumner Jason Yaffe was born in Boston, Massachusetts, in 1923, the same year Frederick Grant Banting and John James Rickard Macleod received the Nobel Prize for discovering insulin, Edward Hubble confirmed galaxies exist beyond the Milky Way and Roy and Walt Disney founded the Walt Disney Company. His parents owned a retail shoe store. He attended the Boston Latin School, the first and oldest public school in this country, founded in 1635. Notable graduates from the school included John Hancock, Samuel Adams, and Benjamin Franklin.

At age 18, Sumner enrolled at Harvard College, but his college studies were shortened in 1943 when he became eligible to be drafted for service in the armed forces (Figure 2). He applied and was selected for duty in the Office of Strategic Services, the forerunner of the Central Intelligence Agency. As part of his military duty, he attended Berkeley to learn Chinese and ultimately became proficient in this most difficult language. His assignment as a member of the Special Forces was to be dropped behind enemy lines in China during World War II. The war, however, ended before Sumner could practice his Chinese, and in 1945, he returned to Harvard College where he earned an AB degree in chemistry. It was at this time that he decided to

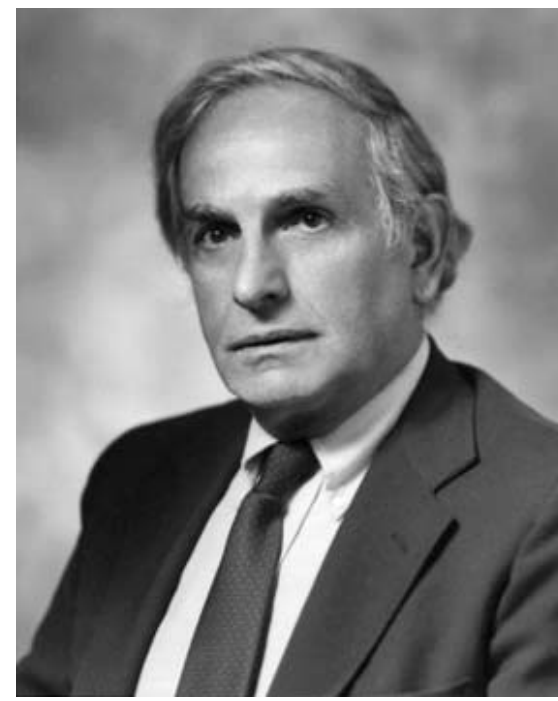

Figure 1. Sumner J. Yaffe, MD, The Father of Pediatric Clinical Pharmacology.

Figure 2. Sumner Yaffe around the time he entered Harvard College.

Figure 3. Sumner graduating from Harvard College, MA in Pharmacology.

Figure 4. Dr. Yaffe during his fellowship in metabolism with Dr. Schwartz at Boston Children's.

Figure 5. Dr. Yaffe addressing an international conference.

pursue pharmacology research at Harvard University, studying age-dependent differences in cardiac responses to digitalis. This investigation marked the beginning of a lifelong interest in the influence of ontogeny in drug disposition and effect. Sumner then earned an MA degree in pharmacology and decided to become a physician, graduating from the University of Vermont in 1954 (Figure 3). He completed his pediatric internship and residency at Boston Children's Hospital, after which he received a Fulbright scholarship to study hypercalcemia and its relationship to vitamin D overdose at Saint Mary's Hospital, London, England. He returned to Harvard for a fellowship in metabolism under Robert Schwatz. After completing this fellowship, he joined the faculty at Stanford University, becoming the Program Director of the Clinical Research Center for Premature Infants (Figure 4). It was then that he developed an interest in neonatal pharmacology and became involved in a number of studies of the clinical pharmacology of antibiotics in preterm infants. Both investigative and practical, his work featured clinical correlations, as reflected in an early publication focusing on effectively controlling staphylococci in the nursery.[1]

In 1963, Sumner moved to Buffalo Children's Hospital, as Director of the Division of Clinical Pharmacology and Professor of Pediatrics and Adjunct Professor of Biochemical Pharmacology at University at Buffalo, the State University of New York. Recognizing the need to introduce the clinical community to the fledgling specialty of pediatric clinical pharmacology, while demonstrating value at the bedside, Sumner published initial early reviews advocating the use of pediatric clinical pharmacology.[2–5] In 1969, Sumner was awarded a special National Institutes of Health (NIH) fellowship to travel to Sweden as a visiting Professor of Pharmacology at the Karolinska Institute. In 1975, he accepted a position at the Children's Hospital of Philadelphia as head of the first division of pediatric clinical pharmacology at that institution.

During his distinguished academic career, he was committed to education and the sharing of new findings, publishing more than 300 scientific articles and books dealing with a wide range of developmental science. The ontogeny of drug-metabolizing enzymes was a primary focus of Sumner's intense research interest. His creativity in clinical research, grounded in clinical applicability, is clearly visible in his 1964 publications addressing glucuronyl transferase[6] and sulfate metabolism.[7] He was among the first researchers to study these enzymes in various human fetal tissues and in placenta.[8] Furthermore, he was very interested in unraveling the effect of various factors on the drug metabolizing enzyme systems of the developing organism. Sumner made original contributions to knowledge of the effects of protein intake, malnutrition, metals, vitamins, and hormones on hepatic drug metabolism.

Other original contributions include mechanistic studies of the teratogenic effect of xenobiotics and the long-lasting cerebral effects of fetal exposure to

sex steroid hormones. Early in his career, he embraced toxicology as an extension of clinical pharmacology, again focusing on improving the care of children. In 1964, he published a clinical and pathological assessment of a fatal case of amitriptyline poisoning.[9] In addition to these cutting-edge accomplishments, Sumner was involved in studies of the clinical pharmacology of various drugs, the effect of phototherapy on bilirubin metabolism, and the excretion of drugs in breast milk. Two of his enduring works have received worldwide recognition as key pediatric pharmacological references, *Drugs in Lactation* (with Gerald G. Briggs and Roger K. Freeman) and *Pediatric Pharmacology* (with Jacob V. Aranda).

After many scientifically fruitful years, Sumner entered the arena of administration, when in 1980, he accepted the Directorship of the Center for Research for Mothers and Children (CRMC) at the National Institute of Child Health and Human Development (NICHD), a position that had been vacated by Jonathan Lanman. During his 20-year tenure, Sumner influenced and molded research policies at the CRMC of the NICHD. His genius was in combining an insatiable scientific curiosity with a vision of how research could be accomplished. As Director of CRMC, Sumner was responsible for a multimillion-dollar research portfolio consisting of disciplines as disparate as child psychology and teratology.

Sumner had a keen ability to identify promising young researchers and to guide them to appropriate funding opportunities and in many cases creating such opportunities. He was a consummate teacher. Of paramount importance to the pediatric clinical pharmacy and clinical pharmacology communities are the results of his pioneering efforts in the development of clinical research networks at NICHD, at a time when clinical research was frowned upon by the mainstream NIH and considered a minor discipline. He created the Neonatal and Fetal Maternal Medicine networks, now in their 25th years of operation. Despite the demands of the job, Sumner found the time and will to constantly and aggressively advocate for the study of drugs in children.

In 1990, the Forum on Drug Development of the Institute of Medicine (IOM) sponsored a workshop to address the serious issue of the lack of pediatric labeling. Sumner was instrumental in convening the key stakeholders, NICHD, Food and Drug Administration, pharmaceutical companies, and academia, to thoughtfully address this long-standing omission. Recommendations from the workshop were made to the four parties involved. Adoption of two of the IOM recommendations had far-reaching consequences, including the creation of 1) incentives to promote innovator-sponsored labeling drug studies earlier in the drug development process, and 2) a network of Pediatric Pharmacology Research Units (PPRUs) to demonstrate that comprehensive, information-rich labeling studies could be performed in children of all ages, including those who are critically ill. The success of this network has become his crowning achievement.

Figure 6. Sumner Yaffe on holiday with daughter Kristina on Martha's Vineyard.

For many years, Sumner was the articulate spokesman for pediatric clinical pharmacology in national and international forums. In donning this mantle, he traveled to all corners of the world (Figure 5). These sojourns blended very nicely with his penchant for international travel in pursuit of improved heath care for children. He served with distinction as chair of the Committee on Drugs of the American Academy of Pediatrics and devoted time and energy to many scientific advisory committees and innumerable academic and professional associations. Sumner recognized early in his career the importance and immense value of the

interprofessional team in improving clinical care and, in particular, the important role of the pediatric clinical pharmacist. Sumner was a leader in including the clinical pharmacist in all aspects of pediatric research and clinical care and fought hard for equal access to competitive grant funds. These attributes have been recognized by the Pediatric Pharmacy Advocacy Group and have served as the foundation for the development of the Society's annual Sumner J. Yaffe Lifetime Achievement Award, an award recognizing preeminent individuals for their significant and sustained contributions to the improvement of children's health through the expansion of the field of pediatric pharmacology and therapeutics. Shortly after being the first recipient of this prestigious recognition, he told one of the current authors (MDR) that this award was the most meaningful to him, among all the awards he had received during his career.

It would be impossible to accurately describe Sumner without talking about his private side as a doting and loving father. His zest and enthusiasm in his professional life was also manifested in his playful activities with his children, particularly at their yearly summer vacation home on Martha's Vineyard Island. Kritina, Sumner's first-born daughter, followed in her father's footsteps and has become an accomplished physician scientist on the staff of neurology faculty at University of California at San Francisco (Figure 6).

Sumner is survived by his beloved wife Sussane, five sons, one daughter, and five grandchildren.

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