Obituary of Dr. Andrew G. Engel

It is with deep sadness that we share the news of the passing of Dr. Andrew Engel, one of the most revered and influential figures in the field of neuromuscular disease. His loss is a profound one, and his contributions to our specialty will be remembered for generations to come.

Dr. Engel was born in Budapest, Hungary, and immigrated to the United States in his teens with his family. He earned the MD degree from McGill University in 1955 with a gold medal for achieving the highest academic standing upon graduation. After an internship at the Philadelphia General Hospital, he began an internal medicine residency at the Mayo Clinic, but his training was interrupted in 1958 when he had to sign up for National Service. He chose the US Public Health Service where he was eventually assigned to the Division of Neurology directed by G. Milton Shy at the National Institutes of Health. During this period, he decided to become a neurologist. In 1960 he returned to the Mayo Clinic to complete his training in Internal Medicine and Neurology. From 1962 to 1965 he was a postdoctoral fellow in Neuropathology at Columbia University in New York. In 1965, Dr. Engel was appointed to the Staff of the Mayo Clinic in Rochester MN.

Dr. Engel is an internationally renowned neuromuscular clinician, educator, and researcher whose impact on the field truly cannot be overstated. He has been a beacon of excellence in the field of neuromuscular diseases, cherished by patients as an astute and caring clinician, nurturing numerous fellows as a dedicated mentor and teacher, and sharing his expertise in muscle pathology, biochemistry, electrophysiology, and molecular genetics. Dr. Engel discovered many novel neuromuscular diseases and unraveled the pathogenesis of many others and his contributions to the field over many decades have been extraordinary.

Dr. Engel has written more than 350 peer-reviewed papers, numerous reviews, and has edited and been a key contributor to three editions of *Myology*, the most highly regarded text in the field. He has made numerous impactful contributions to neuroscience and the following provides a brief summary. His early contributions included the discovery of multicore disease, fingerprint body myopathy, sarcotubular myopathy, and late-onset nemaline myopathy. Subsequently, he also discovered late-onset acid maltase deficiency, and a lipid storage myopathy due to carnitine deficiency. He identified the first instance of human Coenzyme Q10 deficiency as the cause of a lipid storage myopathy and encephalopathy. He worked with Dr. Ed Lambert in hypokalemic periodic paralysis and established that failure in excitation-contraction coupling resided in the muscle fiber surface membrane. Antedating by many years the discovery of dystrophin, and against much skepticism at the time, he described the membrane defects in Duchenne dystrophy and postulated that the basic abnormality in the disease resided in the surface membrane of the muscle fiber. Again, working with Dr. Lambert, he made several key contributions to the pathology and immunopathology of human and experimental myasthenia gravis and described the phenotypes of the slow-channel syndrome and congenital endplate acetylcholine esterase deficiency. His freeze-fracture and immunoelectron microscopy studies, some done with Dr. John Newsom-Davis, defined the voltage gated calcium channel of the presynaptic membrane as the target of the autoimmune attack in the Lambert-Eaton myasthenic syndrome. Subsequently, he explored the immunopathology of different inflammatory myopathies, and described T-cell mediated muscle fiber injury in polymyositis and inclusion body myositis. Dr. Engel then used molecular genetics techniques combined with electrophysiology, and

discovered the molecular and genetic basis of endplate acetylcholinesterase deficiency and elucidated the pathology, pathophysiology, molecular genetic basis, and therapy of a series of congenital myasthenic syndromes. He also defined the morphologic phenotype of myofibrillar myopathies that subsequently led to the discovery of mutations in myotilin and a Z-disk associated protein, ZASP, and BAG3.

Dr. Engel's remarkable accomplishments in the field have been recognized with a multitude of awards and accolades, including Jacob Javits Neuroscience Investigator Award twice, the Duchenne-Erb-Prize of the German Muscular Dystrophy Group, the Jerry Lewis Research Award from the Muscular Dystrophy Association, the Carrell-Krusen award from the Texas Scottish Rite Hospital for Children, the Bernard Sachs Award of Child Neurology Society, the Gaetano Conte Prize of Mediterranean Society of Myology, and the Lifetime Achievement Award for Neuromuscular Diseases by the World Federation of Neurology. In 1994, he presented the prestigious Wartenberg lecture at the American Academy of Neurology and in the same year the Mayo Clinic honored him with the Distinguished Investigator Award. He has been awarded honorary membership in the AAN, ANA, and the European, German and Spanish Societies of Neurology. In 2003, he was elected to the Institute of Medicine of the National Academy of Science.

We extend our deepest gratitude for Dr. Engel's remarkable mentorship, unwavering friendship, and tireless dedication to advancing the field of neuromuscular disease. It has been an extraordinary privilege to learn from and work alongside such a distinguished colleague. Though his absence will be deeply felt, Andy's legacy endures through the many lives he touched—his colleagues, collaborators, the countless mentees he inspired and most importantly the many patients he helped both here at Mayo Clinic and across the world.

Sincerely,

Sean Pittock, MD, Chair, Department of Neurology
Michelle Mauermann, MD, Chair, Division of Neuromuscular Medicine
Duygu Selcen, MD, Division of Child and Adolescent Neurology
Maureen Prunty, Operations Administrator, Department of Neurology

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