THE FACULTY OF MEDICINE
Harvard University

Adelbert Ames III

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Adelbert (Del) Ames III, Professor of Physiology, Department of Neurosurgery Massachusetts General Hospital (1969-1991) and the Charles Anthony Pappas Professor of Neuroscience, Harvard Medical School, Massachusetts General Hospital (1983-1991) Professor Emeritus (1991-2018) died on May 31, 2018 at the age of 97.

Born in Boston, MA on February 25, 1921, to Fanny Vose Hazen Ames and Adelbert Ames Jr., son of the civil war general of the same name. He and his sister Priscilla grew up in Hanover, New Hampshire. He fished, hunted and was an avid bird watcher. He skied at the Nations first rope tow in Woodstock Vermont and skied in his first Hochgebirge Challenge cup race at Cannon Mountain, New Hampshire at the age of 13. He successfully continued competitive skiing until almost 90 years old. Del moved from Hanover High School to Exeter Academy (Class Valedictorian, 1939) and graduated from Harvard College,1941(Phi Beta Kappa).

He was then educated at Harvard Medical School (graduated cum laude, elected to Alpha Omega Alpha) and served in the Army doing research in Alaska on how to keep troops alive in extremely cold conditions. After obtaining his medical degree from Harvard Medical School in 1945, he completed a medical internship and residency in internal medicine at the Presbyterian Hospital in New York City from 1945-1952 and was a Research Associate at Harvard Medical School from 1952-1969. He became a Professor of Neurophysiology in the Department of Surgery, Harvard University, Boston, and was recruited to the Neurosurgical Service at MGH by Dr. James White who was chair at the time. He held the titles of Neurophysiologist in Neurosurgery and the Charles Anthony Pappas Professor of Neuroscience at Massachusetts General Hospital and Harvard Medical School, Boston, respectively, from 1983-1991, from which he retired as professor emeritus.

Dr. Ames III or "Del", as he was fondly known by colleagues and friends, was a true gentleman, kind and generous with others and humble, reflective and thoughtful. He was a supportive mentor to many medical students, physicians, scientists and surgeons up to the new millennium and well beyond. He would invite colleagues to his home in Vermont where he lived life with his wife, Polly Jenckes, and discuss science, education, life and balance. Former mentees describe him as, "*a light when darkness prevailed*", and

"*brilliant and always took the time to believe in a young student*".

His passion for brain research actively continued for many years after his official retirement, in 1991, and he continued to author and review journal articles up to 2011.

During the course of his career, Ames was also a notable member of various professional societies including the American Physiological Society, American Society for Neurochemistry, Society for Neuroscience, and the International Society of Neurochemistry.

Fundamental discoveries related to the brain

Del Ames contributed significantly and fundamentally to biomedical research and it would take several pages to do proper justice to his entire body of work. In this article, we chose to highlight three (3) of his most important discoveries, (1) the no-reflow phenomenon, (2) Ames' medium and (3) how to protect brain tissue by rectifying the energy imbalance that occurs during cerebral ischemia.

No-reflow phenomenon

The phrase "*no-reflow phenomenon*" was first coined, discovered and reported in the rabbit brain by Ames and colleagues in the illustrious journal, The Lancet (Majno, Ames III, Chiang, et al., 1967). It is of interest that this letter in The Lancet was based on a series of experiments that had not yet been published. The results were published the following year. In this set of observations, Ames and colleagues examined the changes in brain blood vessels (small and large) in 62 rabbit brains exposed to 2.5, 5, 7.5,10, and 15 minutes of ischemia. At the end of the ischemic period the brains were perfused with carbon black and examined for absence of vascular filling, or perfused with Ringer's solution and examined for trapped blood. By both methods, localized areas were found that had failed to admit the perfusion fluid. The earliest lesions were small and involved only the microvasculature. As the duration of ischemia was increased, the amount of tissue affected by the vascular obstructions also increased, reaching in some cases 95% of the brain after 15 minutes of ischemia. Therefore, vascular narrowing was shown to constitute the first irreversible changes during ischemia. Subsequently, over the next 10 years this discovery was validated in the brain of several other animal models. Moreover, beyond the brain, this fundamental discovery was later shown to exist in several major organs in mammals including the heart, kidney, skeletal muscle and skin. In addition, this laboratory finding is now well established as having fundamental clinical significance, not only in cerebral ischemia, but also in acute myocardial infarction in humans (Rezkalla and Kloner, 2002).

Ames' Medium and the Rabbit Retina Model

During his early research career, Del established an ingenious physiologic model of the brain using the rabbit retina. Initially, he studied cerebrospinal fluid from the brain and eventually created an artificial version of this remarkable brain fluid referred to as Ames' Medium (Ames and Nesbett 1981). He used this medium to show that it was possible to support integrated electrophysiologic and metabolic retinal function for more than 2 days, exemplified by responses to photic stimuli. Today this mixture remains the medium of choice for maintaining central nervous system tissue *in vitro*. The rabbit retina model itself was eventually also reported in the medical literature (Quiñones-Hinojosa et al., 1999). He subsequently developed a model of ischemia using the retina to measure metabolic and physiologic function of neural tissue, measured from light-evoked compound axon potentials from the optic nerve ex vivo and exposing it to ischemic insults by depriving it of glucose and oxygen.

Brain protection

Having identified a major principle underlying damage caused by cerebral ischemia pathophysiology, as well as a model in which to study the brain, Ames set out to try to find a way to prevent the brain from injury due to stroke. He reasoned that damage caused by cerebral ischemia resulted from an imbalance between the reduced energy supply caused by ischemia and the high neural energy demand. Consequently, rectifying that energy imbalance during cerebral ischemia should result in brain protection. Ames tested this hypothesis with his usual fundamental approach, by developing a unique pharmacologic cocktail, designed to reduce brain energy demands by blocking temporarily non-critical neuronal function (Ames et al., 1995). It took a tremendous number of experiments analyzing each potential protective agent on its own and then in graded combination with other agents. This 'cocktail' was subsequently used to show that damaging anatomical effects of stroke (i.e., cerebral infarcts) could be avoided or reduced in a major way, during cerebral arterial occlusion by temporarily blocking neuronal functions in the rabbit (Maynard et al., 1998). This outcome was repeated from a metabolic and functional perspective using hypothermia in the rabbit retina model (Quiñones-Hinojosa et al., 2003).

The impactful contributions of Del Ames to the scientific and medical community continue to play an important part of neuroscience, neurology and neurosurgery across the US and around the world. Moreover, the impact he had on people, i.e., his family, friends, mentees and peers, exemplified by his commitment to personal excellence whether in science or sport, his curious nature, this life-long learner and humble gentle-giant will live forever in our hearts and minds.

Respectfully submitted,

Christopher S. Ogilvy, MD (*Chair, Ames Memorial Minute Committee*)
Bob S. Carter, MD, PhD
Kenneth I. Maynard, PhD
Eric L. Zager, MD
Nicholas T. Zervas, MD