Edward H. Oldfield, MD, passed away on September 1, 2017. His death was a significant loss to everyone that knew him, including the over 100 trainees that he mentored from around the world. While neurosurgery has lost a giant, Ed's life left an indelible mark through scientific discovery and surgical innovation, as well as generations of trainees and colleagues.

On September 1, 2017, Edward Hudson Oldfield, MD, passed away peacefully at his home surrounded by his wife (Susan) and daughter (Caroline). After a courageous and hard-fought battle, his life was cut short by melanoma. However, Ed left a permanent legacy in our specialty that included critical scientific discoveries and surgical advances that led to improved patient care. Not only did Ed leave an indelible mark on the field of neurosurgery and the broader medical profession through these discoveries and innovations, he shaped a generation of neurosurgeons who had the opportunity to be mentored by him. His success as a surgeon, scientist, and mentor were the result of personal characteristics and attributes that were forged through a broad range of life experiences.

BIOGRAPHICAL BACKGROUND

Ed was born in the small town of Mount Sterling, Kentucky, on November 22, 1947 to Ellis and Amanda (née Miller) Oldfield. He was the second of 5 children, with 1 older sister, as well as 2 younger brothers and 1 younger sister. Ed's father was a decorated World War II veteran having been awarded 2 Bronze Stars and a Purple Heart. His father lost his leg above the knee during the war from injuries sustained from German machine gun fire in France several weeks after the Normandy invasion. After returning from World War II, Ed's father came back to Mount Sterling, married his mother Amanda, and opened a car dealership. After watching his father persevere and overcome despite a disabling war injury, Ed developed a deep sense of determination, gratitude, and a tenacious spirit.

Sadly, Ed's father would pass away when he was 11 years of age from pancreatic cancer. Ed was very close to his father and deeply affected by his death. He attributed many of his own intellectual gifts and motivation to his father. After his father died, to support the family, Ed's mother became a schoolteacher. She was highly educated and the only woman in the 5 eastern counties of Kentucky at that time to have a Master's Degree. His mother never remarried and raised Ed and his siblings alone. Ed's early life experiences, along with his father and mother's influences, shaped his character. These forces resulted in Ed's potent sense of fairness and self-reliance, as well as an unyielding work ethic, a profound intellectual curiosity, a sense of self-introspection, and humble demeanor.

After high school, Ed left Kentucky to attend college and study physics in a work-study program between Oak Ridge National Laboratories and Georgia Tech. Early in his first year, Ed was placed at the super conductivity laboratory at the Oak Ridge National Laboratories in Tennessee. The laboratory that he worked in there had no windows and little human contact. After 1 semester, Ed became homesick, quit, and returned home to work. He worked road construction building the I-64 highway though his home counties in Kentucky. He later worked on a survey crew in the rugged
mountains of southeast Kentucky. After living above a bar with a 40-year-old alcoholic college dropout workmate in whom he saw wasted intelligence, Ed resolved not to waste his own. He enrolled at University of Kentucky the next year.

At the University of Kentucky, Ed continued to study physics. However, during his first year of college at the University of Kentucky, Ed took an aptitude test to help define a best potential career match. Even then, aptitude testing revealed he was best suited to be a surgeon and he began to consider a career in medicine. While at the University of Kentucky, Ed would meet Susan, the love of his life and future wife. Ed completed 3 years of college and then matriculated directly into the University of Kentucky College of Medicine without graduating with an undergraduate degree. While at the University of Kentucky College of Medicine, Ed would excel academically on his path to obtaining his medical degree.

Ed moved to Vanderbilt University Medical Center in Nashville for his neurosurgical training after medical school. Upon completing his intern year, Ed asked Susan (née Wachs) to marry him. They married (1974) in her hometown of Lexington. Department Chair, Bill Meacham, MD, and Cully Cobb, Jr, MD, were Ed’s early mentors during residency at Vanderbilt. These surgeons were critical in developing Ed’s surgical skills and supporting his intellectual curiosity. During residency, Ed completed his neurology rotation at Queen Square in London, England. While at Queen Square, Ed worked with Valentine Logue, MD, who had a critical impact on his career and honed his examination and observational skills. These skills would later lead to the origin of a number research studies derived from clinic and operating room findings.

After finishing residency in 1980, Ed joined Lexington Neurosurgical Associates, an outstanding private practice in Lexington, Kentucky. There he enjoyed practicing neurosurgery and working with his partners, William Brooks, MD, and Russell Travis, MD, (American Association of Neurological Surgeons (AANS) President, 1998-1999). James Bean, MD, (AANS President, 2008-2009) would also later join this practice. Nevertheless, Ed had an unquenched interest to combine his surgical practice with research. It was his partner and friend, Bill Brooks, who encouraged him to look at academic opportunities, including the National Institutes of Health (NIH; a place Ed had not heard of until that time). After 1 year in private practice, he accepted a position at NIH.

In 1981, Ed started work in the Surgical Neurology Branch at the NIH, as a Senior Staff Fellow. Five years later, Ed would become the Chief of the Surgical Neurology Branch. For the next 21 years, Ed led the neurosurgery effort for the NIH as Branch Chief. While at the NIH, he developed and expanded research programs in Chiari I malformation, syringomyelia, epilepsy, neuro-oncology, drug delivery, and spinal vascular malformations. His leadership and multidisciplinary collaborations were the drivers of the success in these programs. Physicians and scientists from the basic, translational, and clinical areas all enriched these programs. Under his leadership, deeper understanding of the neurological disorders that were investigated led to new biological insights and enhanced patient care. Susan and Ed’s daughter, Caroline (1989), would also be born during their time at NIH.

Ed moved to the University of Virginia in 2007 and spent the final 10 years of his career there as the W. Gayle Crutchfield Chair in Neurological Surgery. At the University of Virginia, Ed led a multidisciplinary pituitary and neuroendocrinology team. He continued to investigate many of the same neurological disorders that he did at the NIH, including Cushing disease, convection-enhanced delivery, Chiari I malformation, and syringomyelia. Specifically, he continued to publish original and influential papers in these research areas. While at University of Virginia, Ed remained immersed in mentoring residents, fellows, and junior faculty until he passed away. Throughout his career, Ed was generous with his time and grateful of others’ time. He was always willing to engage committed individuals interested in neurosurgery and the related sciences.
Unique in this era of medical discovery, Ed made significant scientific contributions across a broad range of topics. These areas of research primarily included spinal vascular malformations, Chiari I malformation and syringomyelia, pituitary adenomas, drug delivery, nervous system neoplasia, gene therapy, and vasospasm. The contributions to these areas spanned the basic, translation, and/or clinical sciences and often represented large multidisciplinary efforts. Based on Ed’s collaborative work, these studies culminated in over 500 scientific and clinical publications, an h-index over 100, and over 43,000 citations.

Spinal Vascular Malformations
Ed, working with 2 outstanding interventional radiologists Giovanni DiChiuro, MD, (first to perform spinal arteriography) and John Doppman, MD, was critical in differentiating the biological and clinical features of the spinal dural arteriovenous fistulas and arteriovenous malformations.1-4 Biologically, they defined and differentiated spinal dural arteriovenous fistulas, which they found were acquired lesions, from arteriovenous malformations, which are congenital.1 These features had implications that they used to inform the natural history, radiographic findings, clinical findings (differing mechanisms of neurological deterioration) and methods of treatment. At that time, they revealed that simple interruption of the intrathecal venous drainage of the spinal dural arteriovenous fistula was a permanent, safe, and effective way to treat these lesions.3,5

Chiari I Malformation and Syringomyelia
Based on cine-magnetic resonance imaging, Ed and a team of NIH investigators defined the underlying pathogenesis of Chiari I malformation-associated syringomyelia.6 Specifically, they discovered that blockage of cerebrospinal fluid flow at the level of the foramen magnum by downward displacement of the cerebellar tonsils during systole produced a systolic pressure wave in the spinal cerebrospinal fluid that acts on the surface of the spinal cord. The pressure wave results in initiation and progression of syringomyelia by the pulsatile pressure waves forcing cerebrospinal fluid into the cord through the perivascular and interstitial spaces. These findings later lead to the refinements in the surgical management of Chiari I malformation, as well as insights into primary/secondary causes of syringomyelia and their natural history.7-9

Pituitary Tumors
While at the NIH, Ed was immersed in an internationally recognized group of pituitary endocrinologists. This team would investigate the clinical, laboratory, imaging, and surgical features of Cushing disease. This multidisciplinary effort leads to the development of inferior petrosal sinus sampling (most accurate diagnostic test for Cushing disease),10 defined diagnostic testing (laboratory and imaging) for diagnosis,11-13 testing to assess for biochemical remission,14,15 guidelines for management,16 pathological/histologic features,17 and surgical technique.18 Surgically, the description of the histologic pseudocapsule was exploited for improved resection of adenomas, enhanced assessment of contiguous dural invasion, and improved pituitary gland functional preservation.15,19

Drug Delivery
After observing that edema surrounding metastatic deposits could drive small and large molecules over large distances in the extracellular space, Ed and 2 bioengineers (Paul Morrison, PhD and Robert Dedrick, PhD) developed and modeled the concept of bulk flow, or convection-enhanced delivery, to distribute small and large molecular weight compounds in the interstitial spaces of the nervous system via a small
hydrostatic pressure gradient.20 This led to the investigation and discovery that convection-enhanced delivery could be used as a method to bypass the blood–brain barrier and directly deliver putative therapeutic compounds in a reliable, homogeneous manner over large regions of brain, brainstem, spinal cord, and peripheral nerves for potential treatment of a variety neurological disorders.21-28

**Nervous System Gene Therapy**

In the early 1990s, gene therapy was unchartered territory that carried new hope for innovative therapeutic options. Nevertheless, it was associated with considerable unknown risks. In collaboration with the National Cancer Institute, Ed investigated this new technology and was the first to use in vivo transfer of a therapeutic gene (Herpes simplex thymidine kinase gene delivered via intratumoral implantation of retroviral vector-producer murine cells) to treat brain tumors.29,30 After an arduous approval process, the first gene therapy trial in patients with primary and metastatic brain tumors was started at NIH.31-33 This study led to subsequent studies and delineated the hurdles and limitations of therapeutic gene transfer, paving the way for the slow and difficult road for modifying the human genome for therapeutic measures.

**Nervous System Neoplasia**

Ed made critical contributions to the understanding of central nervous system neoplasia (benign and malignant) in several areas. He and members of the Surgical Neurology Branch defined the role of vascular endothelial growth factor in (initially known as vascular permeability factor) the development of edema and neovascularization in the central nervous system, as well as the mechanisms of edema reversal via dexamethasone.34-37 He led efforts to define the biological features, natural history, and optimal management of central nervous system lesions (hemangioblastomas and endolymphatic sac tumors) in von Hippel–Lindau disease.38-44 Ed also pioneered the treatment of glioblastoma using convective delivery of putative therapeutics, including immunotoxins, chemotherapeutic agents, and gene vectors.26,27,45

**Vasospasm**

Prior work had revealed that nitric oxide was critical for maintaining cerebrovascular tone. In subarachnoid hemorrhage, oxyhemoglobin rapidly binds nitric oxide indicating that nitric oxide may be involved in the pathogenesis of cerebral vasospasm. Working with investigators within the Surgical Neurology Branch, Ed and colleagues further investigated the role of nitric oxide (or loss of) in cerebral vasospasm after subarachnoid hemorrhage. They found that intracarotid infusion of nitric oxide could reverse vasospasm.46,47 These findings led to the use of nitrite infusion (a source of nitric oxide) to prevent delayed cerebral vasospasm in nonhuman primate models of subarachnoid hemorrhage.48 These data have led to human clinical trials using nitrite infusion after subarachnoid hemorrhage to prevent vasospasm.49,50

**MENTOR AND ROLE MODEL**

The most significant impact a medical professional can make during their career is through shaping the future clinical, scientific, and humane virtues of their trainees. This is commonly referred to as mentorship. Under his guidance, Ed transformed the professional and personal lives of over 100 surgeons and scientists who were fortunate to share his knowledge, insights, intellectual curiosity, as well as the occasional criticism given in a deceivingly mild southern drawl. Ed had no patience for a careless, sloppy, or less than perfect approach to surgery or science. His pupils all remember the generosity with his time that he devoted to them, discussing research projects, analyzing data, and forming conclusions into a scientifically sound report. These discussions were an
evolving process, in which he shared philosophical pearls, as well as tips on fly-fishing, that were eternally carved into our personalities.

To gain Ed’s respect, you had to work very hard. In fact, we all did. He set the bar high, but passing that bar was a source of satisfaction and pride rarely experienced before knowing Ed. Ed was not a middleman. He was always engaged and focused on the task at hand. His views and impressions on people and issues were clearly stated in a polite, but unapologetic and unambiguous, way. You could agree or disagree with his views, but you always took them seriously, because they often provided new, unnoticed perspectives and insights. Ed's mentoring did not stop once you left this direct tutelage. In fact, it continued throughout his lifetime and continues today for all his trainees. Education and mentoring of new generations of neurosurgeons around the world by his former students maintain his legacy. This legacy of Ed is a true source of envy to any neurosurgeon who strives to make an impact on our profession.

Based on Ed's mentorship, many of his former students have made successful careers in neurosurgery, becoming department heads, professors, and accomplished scientists around the globe. Invariably, all his trainees have maintained close ties with Ed, his wife Susan, and his daughter Caroline (whom some of us have known from infancy). All his mentees have cherished their friendship with him. Such camaraderie is unusual in the world today. Nevertheless, it is a tribute to the exceptional character and personality of Ed Oldfield, the man and surgeon. Neurosurgery is a technical profession and Ed was, undoubtedly, a master surgeon in his fields of expertise. However, what we have gained from knowing Ed and working with him is so far more than just surgical and research skills. We feel fortunate to having had such an opportunity and being able to say, “I have trained and worked with Ed Oldfield.”

CONCLUSION

Ed’s scientific and surgical influences have left a permanent mark on critical areas that impact neurological surgery and, more broadly, the medical profession. While these contributions have permanently shaped our understanding of neurological disease and patient management, the mentorship that Ed provided to medical students, residents, fellows, and faculty is the thread that will bind and shape the field for many generations to come.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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REFERENCES


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