

Mr. Piano Man: Reflections on the Life of Physician, Scientist, and Humanitarian, William L. Young, MD (1954–2013)

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We hope Bill Young would have enjoyed this title. Being a musician was the alter ego for this exemplary physician-scientist, and treasured friend and colleague, in our neuroanesthesia and neuroscience communities.

William L. Young, MD, passed away on August 1, 2013. He fought a battle with cancer that was every bit as heroic as his career in anesthesiology. His death came as a shock to many. He chose to suffer in privacy, his paramount concern being

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to not jeopardize his scientific team and their ability to continue their work in revolutionizing the understanding and treatment of cerebrovascular diseases.

Those who knew Bill, an Indiana native, considered him to be a Renaissance man. While a premedical student at Indiana University he majored in Germanic languages, this being his second choice to music for which he felt noncompetitive at that university's great school of music. Although his interest in medicine prevailed, he became widely known for his jazz piano virtuosity. He also had other broad interests, including philosophy, history, skiing, and travel; these were typically his preferred subjects of conversation (instead of his immense contributions to the science of cerebrovascular disease, a subject on which he had become one of the world's preeminent investigators). He once stated that when he started getting more of his research papers accepted than songs, he knew the direction his life would take. But his diverse background would serve him well in his ground-breaking scientific career.

Bill punched many treasured tickets in his professional life. He was an associate examiner for the American Board of Anesthesiology; served as president of the Society for Neuroscience in Anesthesiology and Critical Care (1996-1997); won the 2009 American Society of Anesthesiologists Excellence in Research Award; was a member of the editorial boards for *Anesthesiology*, *Stroke*, and the *Journal of Neurosurgical Anesthesiology*; and co-edited the *Cottrell and Young's Neuroanesthesia* textbook. He served on many National Institutes of Health study sections. He was a former Professor of Anesthesiology at Columbia University, New York, and later served as Professor of Anesthesia and Perioperative Care and Vice-Chair for Anesthesia Research at the University of California, San Francisco. At the University of California, San Francisco, he also held the James P. Livingston endowed chair. At the time of his death, he was the principal investigator on 5 active National Institutes of Health grants. Late in the course of his disease, he received notification that he again had scored exceptionally well on another National Institutes of Health grant application, written while he battled cancer. He had amassed over 300 peer-reviewed, indexed publications. His untimely death is tragic, but his legacy is profound.

What can we learn from Bill that is special? We think it would be his view, despite overwhelming evidence to the contrary, that he was not special. Like many of us who practice anesthesiology, he was an average student attracted to the "action" part of the specialty. Stimulated by hands-on participation in patient care and the scientific intrigue surrounding that care, he excelled during his residency at New York University. The seeds of his development as a scientist were also modest. He dropped out of his undergraduate chemistry major because he felt he had insufficient math skills to pursue a scientific career. After residency, he was attracted to a neuroanesthesia fellowship at Columbia University because he identified a supportive mentor, Richard Matteo, MD, who, while encouraging Bill to study neuromuscular blockade, placed this fledgling scientist in the domain he would later

reign supreme, that being the neurosurgical operating room. Bill's fortuitous engagements with the experimental cerebrovascular physiologist Shu Chien, MD, and Isak Prohovnik, PhD, a leader in the development of modern methods for measurement of cerebral perfusion, coincided with the nascent field of interventional neuroradiology and the requirement of anesthesiologists to participate in these procedures. Bill brought these scientific tools to the operating room and neuroradiology suite. This caught the attention of the neurosurgery chief, Bennett Stein, MD, who invited Bill to bring his cerebral blood flow measurement apparatus to an arteriovenous malformation (AVM) resection. This resulted in a published case report, his not-so-special first step in a career that would make him the most productive scientist to ever have approached the complex physiology of brain AVMs.

Another lesson Bill taught us was the opportunities created by multilingualism, a likely extension of his undergraduate studies. This aspect of his personality extended beyond his understanding of Germanic and Romance languages to the "languages" of different clinical and scientific disciplines. By learning (and largely teaching himself) the languages of neurology, neurosurgery, neuroradiology, bioengineering, molecular biology, and genetics, he was able to develop and effectively communicate with novel teams of investigators to span the full range from molecules and genomics to physiology and pharmacology to outcomes research. His research led him into largely unexplored pathophysiological territory that involves the intersection of anesthesiology, neurocritical care, and operative neurosurgery. He made revolutionary contributions to understanding a disastrous complication of cerebrovascular neurosurgical intervention called *reperfusion hyperemia* or *perfusion pressure breakthrough*, commonly associated with AVM treatment. In so doing, he helped characterize the basic pathophysiological effects of arteriovenous shunting on cerebral perfusion, intravascular pressure gradients, and cerebral autoregulation. His research group discovered that postoperative hyperemia is not a simple pressure-passive increase in cerebral blood flow. Further, they discovered that regions of the brain rendered relatively hypotensive as the result of nearby high-flow fistulae displayed a remarkable capacity to adapt and shift their autoregulatory curve to a lower set point, thus protecting the normal brain regions from ischemic injury in the setting of an active AVM.

Although Bill's collaborative efforts spanned the entire range of cerebrovascular disease with respect to epidemiology, pathogenesis, risk of hemorrhage, and surgical and interventional radiologic treatments, his latest work will likely be held most important. By studying populations of humans with hereditary risk factors for AVM incidence and hemorrhage, he was able to elucidate the molecular factors that contributed to AVM (and to some extent cerebral aneurysm) development. He discovered that single nucleotide polymorphisms and bone-marrow-derived signaling adversely interact with the biological systems that modulate vascular integrity, so as to promote AVM growth and rupture. This opened the door to the possibility that

genetic screening could allow early detection of those who harbor, or are at risk for, early-stage AVMs. Identification of the lesion at an early-stage of development would allow medical intervention to prevent growth and rupture. To prove this point, Bill's team developed a mouse brain AVM model and provided proof in principal for this concept. Imagine the day when a cerebral AVM or aneurysm becomes a medical, not surgical, problem. Bill did and provided the path to achieve this!

There is another lesson from Bill that we, as anesthesiologists, should inculcate into our culture. Although Bill wrote scores of papers on how to best manage anesthetics for complex neurosurgical procedures, and served as an American Board of Anesthesiology examiner and editor of anesthesiology journals, he did not let his core ethos of being an anesthesiologist restrict his approach to the study of disease states. He felt that we as anesthesiologists need to not only perfect our anesthetic techniques to care for patients with disease, but also study the disease itself so as to eliminate it. He would have been in good company with other historically important physician-scientists such as Jonas Salk and Albert Sabin.

Bill had great respect for those who thoughtfully educated and mentored him, and he was an astute student

of optimal techniques to teach and mentor others. He practiced what he learned, and taught anyone who would listen the importance of firm philosophical foundations when planning ambitious leaps in scientific discovery. He left behind an impressive collection of former students and mentees who benefitted from his counsel and today continue as active and independent investigators.

This humble man who did not major in chemistry because he felt he was not smart enough, and who did not pursue a career in music because he felt he was not talented enough, found a way to change the world. The scientific legacy Bill left us will take another generation or two of scientists to bring it to transformative care. Had he been with us longer, these changes would have come much sooner.

While we friends and colleagues will long respect and admire his many professional contributions, we also feel a personal loss at the departure of this humble giant who was always eager to share a story or laugh, introduce a pithy critique, open our eyes to new ideas, share a book, and—in general—enrich our lives in many other surprising ways. Bill Young was a professional and personality for the ages. We, along with his charming and devoted wife, Chantal, will miss our beloved Mr. Piano Man.