Michael M. Todd, M.D., Recipient of the 2016 Excellence in Research Award

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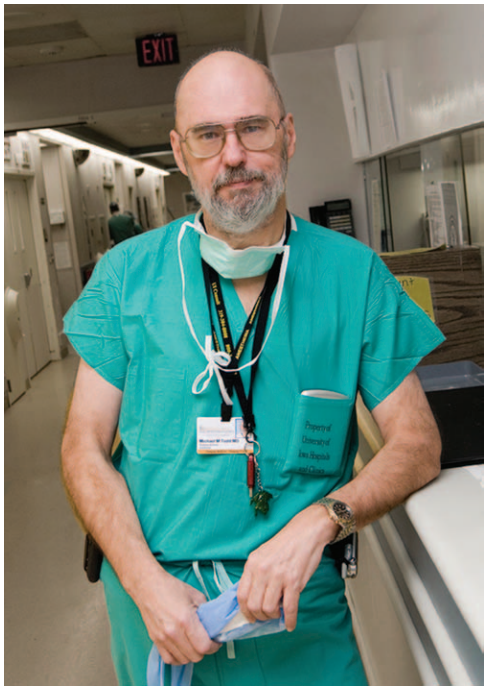
ANESTHESIOLOGY has long prided itself as a clinical discipline based on scientific knowledge. This knowledge has been derived from the contributions of countless individuals who, in small and large ways, aspired to advance patient care through scientific inquiry. This scientific inquiry has most effectively captured the attention of practitioners, and had the greatest impact on patient care, when the investigations challenged anesthesiology traditions that were heretofore based on little or no empirical evidence or were based on liberal extrapolations from experiences in other medical disciplines. Because of absent formal challenges and rechallenges to widely embraced theories and practices, we anesthesiologists have all too often applied weak or incorrect information to patient care.

Michael M. Todd, M.D., recipient of the American Society of Anesthesiologists 2016 Excellence in Research Award, has spent his entire academic career challenging common beliefs and replacing them with improvements based on empirical data. Through his laboratory and clinical investigations, editorial roles in scholarly publications, and the mentoring and encouragement of generations of investigators, Dr. Todd has catalyzed a durable and growing legacy of clinical practice innovations based on scientific principles. His contributions have now spanned 4 decades and reflect many *chapters* of scientific thought and inquiry.



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Foundations

John D. Michenfelder, M.D., is widely considered the father of contemporary neuroanesthesiology in large measure because of his investigational and leadership roles during an august period of neuroanesthesiology progress worldwide. As Dr. Michenfelder's career neared its end, Dr. Todd reached a period of peak productivity and influence and was seen as the next standard bearer who would someday be considered the most influential neuroanesthesiologist in the world. This ascension of Dr. Todd's academic career followed a logical plan. After receiving Bachelor of Arts and Doctor of Medicine degrees from the University of Chicago, Chicago, Illinois, he completed his anesthesiology residency at the Massachusetts General Hospital in Boston, Massachusetts. This was followed by a prestigious elective year as Chief Resident before Dr. Todd moved westward to the University of California, San Diego (UCSD), San Diego, California, to develop his skills in clinical neuroanesthesiology and neuroanesthesiology research under the mentorship of Harvey M. Shapiro, M.D. Dr. Todd remained at UCSD for a total of 7 yr, achieving tenure after only 4 yr on the faculty. While at UCSD, he had rich academic collaborations with Dr. Shapiro, John C. Drummond, M.D., Mark H. Zornow, M.D., and Mark S. Scheller, M.D. In aggregate, these investigators expanded our knowledge and interpretation of physiologic data derived from the Michenfelder era, with a constant eye on improving clinical practice and patient outcomes. Their research employed increasingly refined methodologies to better understand the pathomechanisms and treatment of brain ischemia, anesthetic effects on cerebral blood flow and metabolism (in the context of intracranial hypertension and brain ischemia), and the effects of intravenous fluids on brain edema. This work continues to be highly cited in scholarly publications.

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Dr. Todd then moved from UCSD to the University of Iowa, Iowa City, Iowa, in 1986 to help Chairman John H. Tinker, M.D., rebuild a historically important Department of Anesthesia that had experienced meaningful challenges in recent years.

Iowa—Early Years

Immediately after arriving at the University of Iowa, Dr. Todd established and directed a National Institutes of Health (Bethesda, Maryland)–funded neuroanesthesiology and neuroscience laboratory that was considered among the world's best. Among Dr. Todd's most noteworthy work in this new environment was the discovery and elucidation that the clinical practice of severe fluid restriction in the brain-injured patient was not only foolish but potentially injurious. In the laboratory, he meticulously dissected the osmotic and oncotic pressure properties of intravenous fluid replacement therapies and clearly showed that osmolality was the critical driving force for water into and out of the brain. He proved that even in the context of profound reduction in colloid oncotic pressure, no water accumulated in either the injured or the uninjured brain if plasma osmolality was held constant. He also proved that the brain's dependence on osmolality is truly different from other organs, for which water content is most dependent on oncotic pressure. He and his coinvestigators then formulated clinical recommendations that were informed by their exhaustive research. As a result, fluid restriction—which was once a paradigm of clinical practice for neurosurgical and neurologically impaired patients—was largely abandoned worldwide. Instead, intravenous fluid replacement in patients with injured or at-risk brain tissue became more liberalized, and the goals of fluid management now focused on maintaining hemodynamic stability, adequate cerebral perfusion, and stable plasma osmolality (*e.g.*, by using isotonic or near-isotonic crystalloid solutions), all critically important to brain well-being.

During this interval, Dr. Todd also advanced our understanding of anesthetic effects on cerebral blood flow–metabolism coupling and the mechanisms of ischemia-induced brain injury and anesthetic neuroprotection.

During these early years at the University of Iowa, Dr. Todd became increasingly interested in fellowship and collaboration among developing neuroanesthesiology researchers. To address this concept, in 1987, he and former mentee (and now colleague) David S. Warner, M.D., invited two dozen researchers to participate in the first annual meeting of the Unincorporated Neuroanesthesia Research Group (UNRG). These annual meetings became very popular and later morphed into the International Neuroanesthesia Research Group (INRG). The annual meetings rotated locations each year and were always funded entirely by the host institutions. Presentations at early UNRG meetings were limited to evolving research projects (typically for projects or concepts that were experiencing difficulties), and speakers were encouraged to limit themselves to few or no slides. Membership was restricted to those younger than 40 yr, with Dr. Todd being the only exception; however, this rule was soon scuttled when others in the group reached age 40. These UNRG/INRG members later formed the backbone of the International Hypothermia for Aneurysm Surgery Trial (IHAST) investigators (see below, Iowa—Mid-years).

Dr. Todd's investigational maturation at the University of Iowa resulted in a shift from laboratory research projects that focused on parallels in clinical care to original studies in humans. He investigated techniques of tracheal intubation in patients with unstable cervical spines, defined the relative efficacy and utility of the newly introduced alfentanil and sufentanil *versus* fentanyl in patients undergoing craniotomy, demonstrated for the first time the frequency and persistence of pneumocephalus after craniotomy, and dispelled a prevalent belief that the use of nitrous oxide or volatile anesthetics was contraindicated in patients undergoing surgery to treat supratentorial brain tumors. He proved that propofol anesthesia could be safely used for craniotomy (directly resulting in the removal of the black box warning that initially contraindicated its use in these patients) and was instrumental in the introduction of remifentanil into anesthetic practice.

As a result of his many contributions, Dr. Todd became widely recognized as the premier neuroanesthesiologist of his era. He fostered and mentored the careers of many investigators inside and outside his home institutions and, while doing so, taught us two important lessons: First, scientific ideas more effectively develop when people work together. Competition is healthy, but collaboration is more productive. The UNRG/INRG fellowship was just one example, and it fomented countless collaborative research projects and the mutual advancement of many careers. Second, one has the responsibility to lift the whole field. As a member of the editorial board of Anesthesiology, Dr. Todd applied high standards for peer review. However, even in those manuscripts that would be rejected for publication, his reviews were neither harsh nor dismissive. Instead, he always sought a way to use the review process to instruct and support the authors who were trying to contribute new knowledge. Through these lessons, he set the tone for scientific interactions in our specialty. This is best exemplified in the next phase of his career.

Iowa—Mid-years

In the 1990s, mild hypothermia was increasingly explored as a potential neuroprotection therapy in humans. It had long been known that profound hypothermia (in the setting of cardiopulmonary bypass support of circulation) was neuroprotective in humans. However, mild hypothermia was previously thought insufficient to offer protection, in large measure due to a dogged, but incorrect, belief that hypothermia mediated its protection exclusively through depression of supply/demand metabolism. In 1987 and later, research in animal models demonstrated potential protection by lesser temperature alterations during endogenous circulation;

however, the timing of the hypothermia in proximity to the cerebral insult was found to be critical. To expand on early observations in animal models, clinical trials in cardiac arrest, traumatic brain injury, and neonatal asphyxia were mounted to evaluate efficacy.

The University of Iowa has historically been a leader in the study of clinical subarachnoid hemorrhage (SAH), including SAH resulting from leak or rupture of cerebral aneurysms. Review of existing data sets by Dr. Todd and colleagues revealed a high prevalence of new-onset brain injury associated with surgical cerebral aneurysm clipping. This injury plausibly could be amenable to hypothermic protection. Dr. Todd enlisted academicians—most of them UNRG/INRG participants representing multiple institutions—to voluntarily donate their efforts to perform a preliminary randomized human feasibility study of induced mild hypothermia *versus* normothermia in 114 patients who were scheduled for craniotomy and aneurysm clipping surgery. The results were promising, and with this nucleus of investigators, Dr. Todd (as principal investigator)—working closely with University of Iowa colleague Bradley J. Hindman, M.D., and other collaborators from three continents—obtained one of the largest National Institutes of Health grants ever awarded to an anesthesiologist, which, in turn, allowed a multinational team to prospectively enroll 1,001 patients randomized to hypothermia or normothermia during aneurysm clipping. The study was called IHAST, and its insights were greatly needed. Most clinicians had already adopted the use of hypothermia for aneurysm clipping based on animal studies that had nothing to do with SAH. As a result, many neuroanesthesiologists and surgeons worldwide felt that it was unethical to randomize patients to normothermic treatment and—for that reason alone—refused to participate in IHAST!

Contrary to what many expected, IHAST unequivocally proved that there was no benefit from induced mild hypothermia during cerebral aneurysm clipping surgery, and its use has largely been abandoned for this indication. On superficial analysis, IHAST was a failed study, but such an assessment would not be accurate. To begin with, IHAST was a logistical marvel; long-term (*i.e.*, 3 months) neurologic and neuropsychologic data were obtained on 1,000 of 1,001 patients entered into the trial. Such success was without precedent in an National Institutes of Health–funded trial of this complexity, and IHAST to this day stands as the model for how large-scale clinical trials should be conducted in anesthesiology and beyond. However, the positive aspects of IHAST went much further. IHAST was designed to record a wealth of demographic, health status, physiologic, and pharmacologic data on the study patients. This allowed Dr. Todd and his collaborators to, according to plan, scour the data to create a vibrant body of new or incremental knowledge relevant to the outcome from SAH and aneurysm clipping. Twelve publications based on probing of the database, in addition to the original IHAST report published in the *New England Journal of Medicine*, provide some of the best evidence to date on how to care for patients having cerebral aneurysm clipping. Perhaps the most novel finding was the high incidence of sustained incapacitating neurocognitive dysfunction after SAH. The IHAST results have subsequently been widely explored, at a mechanistic level in animal studies, and, collectively, the IHAST-related body of research has fundamentally changed our understanding and practice related to patients who have aneurysmal SAH and require treatment.

Iowa—Later Years

In the midst of conducting IHAST, Dr. Todd became Editor-in-Chief of Anesthesiology. He implemented major changes in the journal's structure and focus and advanced the scientific mission. This role decreased his personal research time, but his contribution to excellence in research continued indirectly as he managed the peer review and publication of many of the most important research articles in our specialty. He also became Chair of the University of Iowa Department of Anesthesia that once again required special insights and intervention to advance its historical role among the more influential academic departments of anesthesiology. In this role, Dr. Todd was extremely successful, as assessed by the validated metrics commonly employed to evaluate clinical and academic excellence.

Despite his heavy administrative roles, Dr. Todd continued to contribute prolifically to our scientific knowledge. His publications included investigations on operating room management and physician performance, resident education, perioperative visual loss, airway management, and biomechanics of cervical spine injury.

Minnesota

Although Dr. Todd's successes and years of academic service would cause many to conclude that his professional career should be nearing its end, Dr. Todd instead determined that he still has much work to do! After serving as chair of an academic department for 11 of his 30 yr at the University of Iowa, he desired a new mission: *i.e.*, one that would allow him to continue his research. Dr. Todd was recruited by Michael H. Wall, M.D., Chair of the Department of Anesthesiology at the University of Minnesota, Minneapolis, Minnesota, to become Vice-Chair for Research, beginning July 2016. This is an extraordinary opportunity for both Dr. Todd and the department. The University of Minnesota has redirected its mission and seeks to increase its prominence as a research-focused medical center. Major resources have been committed to allow Dr. Todd to contribute to the investigative aspirations and accomplishments of yet another academic department of anesthesiology. On the basis of his record to date and the energy and enthusiasm he has for his upcoming challenge—the twinkle in his eye giving us insights into his motivation—we should continue to expect

great accomplishments from him, along with his new colleagues and mentees. We predict that this new era will be no less remarkable than those that preceded it.

Our specialty is blessed with a wealth of exceptional researchers whose science has improved the patient care we provide. Almost all patients we now bring to the operating room leave it benefited, not harmed, by their anesthesia experience. With this continued improvement, investigators today may sometimes struggle to identify and ask the truly important questions needing answers. Dr. Todd has never had a problem finding important questions. Throughout his career, he has focused on diverse and creative methodologies to systematically explore the logic and appropriateness of our anesthesia practice. He has approached his research, and the training of the next generation of anesthesiology investigators, with exemplary scientific rigor, integrity, and a collaborative spirit that promotes widespread engagement and teamwork. The awarding of the 2016 Excellence in Research Award to Michael M. Todd, M.D., brings great joy to the many investigators throughout all of anesthesiology whom he has touched as a scientific colleague, mentor, leader, and friend. More importantly, it recognizes the uncountable number of patients whose perioperative experience has been improved as a result of Dr. Todd's dedication to enhancing the scientific foundations of clinical care.

Congratulations to you, Mike; your friends and colleagues share in this celebration of your many accomplishments.

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Competing Interests

The authors declare no competing interests.

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