David O. Warner, M.D., Recipient of the 2022 Excellence in Research Award

Mark A. Warner, M.D.

It is my sincere pleasure to congratulate Dr. David O. Warner on his recognition with the 2022 Excellence in Research Award received from the American Society of Anesthesiologists (ASA). Dr. Warner has worked in multiple domains to make a difference in our patients' lives. He is highly deserving of this recognition because of the breadth and depth of his research activities and his ability to adapt a variety of research methodologies to pursue important questions.

Dr. Warner received both his undergraduate and medical school education at Ohio State University (Columbus, Ohio). After completing medical school, he spent time as a medical officer at Nigerian Christian Hospital before beginning his residency training at the Mayo Clinic (Rochester, Minnesota). His residency training incorporated a 2-yr research fellowship in pulmonary physiology. His record of National Institutes of Health funding, which continues to the current time, began immediately after joining the Mayo Clinic staff in 1988. He rose quickly through the institution's academic ranks and has been a professor of anesthesiology since 1999.

It is unusual to find a clinician investigator who has such as prolonged record of academic success in multiple domains of study. Dr. Warner's remarkable ability to transition from one important issue to another using diverse and sophisticated research methodologies make him unique. As a practicing anesthesiologist, he closely observes clinical practice, formulates important, clinically relevant questions, and seeks answers. Highlights of Dr. Warner's research and other contributions include the following.

Respiratory Physiology

Dr. Warner's initial research training was in respiratory physiology, benefitting from the combined mentorship of Dr. Robert Hyatt (the father of the pulmonary flow-volume curve) and Dr. Kai Rehder (himself a past recipient of the ASA Excellence in Research Award). Over two decades, Dr. Warner published more than 90 highly cited articles in pulmonary physiology with an initial focus on pulmonary mechanics and respiratory muscle physiology. His findings provided basic insights into normal chest wall function and how anesthesia affects this function. For example, he discovered that anesthesia-induced respiratory depression is caused not by universal depression of respiratory muscle activity but rather by impaired coordination among these muscles. His insights have been of fundamental importance to the daily practice of anesthesia, as respiratory depression continues to be a major source of anesthetic morbidity and mortality.

In addition to studying the effects of anesthetics on chest wall function, he examined the bronchodilatory effects of anesthetics on airway smooth muscle in a laboratory-based program that enjoyed R01 support for over 15 yr. With his Mayo Clinic colleagues Drs. Keith Jones and William Perkins, Dr. Warner discovered that volatile anesthetics relax

Submitted for publication August 6, 2020. Accepted for publication August 6, 2020.

Mark A. Warner, M.D.: Department of Anesthesiology, Mayo Clinic College of Medicine and Science, Rochester, Minnesota.

 Anesthesiology 2022; 137:396–8. DOI: 10.1097/ALN.0000000000004362

smooth muscle both by impairing neural reflexes and by direct effects on airway smooth muscle. Regarding the latter, they demonstrated that volatile anesthetics relax airway smooth muscle by reducing intracellular calcium concentration, as well as myofibrillar calcium sensitivity. Their discovery that volatile anesthetics have the unique ability to relax even maximally stimulated airway smooth muscle (an ability not shared by other bronchodilators such as β-adrenergic agonists) provided a foundation for drug discovery efforts seeking novel bronchodilators.

Perioperative Tobacco Control

While Dr. Warner was pursuing his productive lab-based program, he was also developing additional interests and capabilities in clinical research, founding the Mayo Clinic Anesthesia Clinical Research Unit in 1999. His first major new focus was on perioperative tobacco control, based on his long-standing interest in improving perioperative lung health. With typical enthusiasm, he initiated a comprehensive multidisciplinary tobacco control research program to develop novel practice-based interventions that could help surgical patients quit smoking. He also initiated a line of research to explore the interactions between tobacco use and pain. His work in perioperative tobacco control, which has produced over 70 peer-reviewed publications, has shown that surgery/anesthesia is a "teachable moment" to promote smoking cessation, demonstrated the medical and economic benefits of helping patients stop smoking, and resulted in practical means for anesthesiologists to help their patients quit.

Based on his efforts, anesthesiology and surgical specialties have incorporated tobacco use interventions into clinical practice nationally and internationally, with great benefit to surgical and pain patients. He is recognized as the leading advocate and investigator in perioperative tobacco control, as recognized by his recent election as a Fellow of the Society for Research in Nicotine and Tobacco. He led the Cancer Center Cessation Initiative of the National Cancer Institute at Mayo Clinic to incorporate tobacco treatment into the routine care of cancer patients, successfully implementing a novel "opt out" automatic referral system. Dr. Warner founded the ASA Smoking Cessation Initiative Task Force, dedicated to helping anesthesiologists incorporate tobacco control measures into their practices, so that the evidence generated by his research and others can be widely disseminated and make a real impact in practice. This was a major impetus for his change in scientific direction away from lab-based studies.

Neurodevelopment after Anesthesia and Surgery in Children

Dr. Warner's clinical practice in pediatric anesthesiology raised his awareness of preclinical studies suggesting that the exposure of young animals to anesthetic drugs produced neurotoxicity. He published with his Mayo Clinic colleagues one of the first studies providing evidence that similar effects may occur in children, showing that anesthetic exposure within the first 3 yr of life is associated with a doubling of the risk for the later development of learning disabilities. This initial research has led to a series of 20 publications from his group, including the ongoing National Institutes of Health–funded Mayo Anesthesia Safety and Kids (MASK) study, which provided the first detailed neuropsychological and behavioral phenotype associated with exposure of young children to anesthesia. It is now apparent from the work of Dr. Warner and others that exposure to anesthesia/surgery may be associated with behavioral changes and diminished fine motor skills later in life, especially in those children with multiple exposures. Clearly, this work could have profound implications for children who require anesthesia at a young age and the anesthesiologists who care for them.

Cognition after Anesthesia and Surgery in the Elderly

His interests in how anesthesia and surgery may affect neurodevelopment and concerns raised by animal experiments led Dr. Warner to initiate an integrated series of studies with his collaborator Dr. Juraj Sprung to evaluate the potential impact of anesthesia on the cognitive function of patients at the opposite end of the age spectrum. These studies revealed that although surgery with anesthesia is not associated with an increased risk of clinical diagnoses of long-term cognitive impairment, it is associated with a modest acceleration of cognitive decline. However, similar changes were seen after hospitalization for medical care, intensive care, and after regional anesthesia, making it unlikely that exposure to general anesthesia was causative. Mechanistically, this decline was associated with accelerated cortical thinning in some brain regions but not increased amyloid deposition. These results are reassuring from the standpoint of anesthesia exposure but highlight the continued need to address perioperative brain health, as they confirmed the link between postoperative delirium and long-term cognitive decline.

Innovations in Postgraduate Medical Education and Assessment

Dr. Warner served for 12 yr as a Director of the American Board of Anesthesiology (Raleigh, North Carolina). In that role, he chaired the American Board of Anesthesiology's Research Committee for many years, which produced a series of 20 papers examining the value of both initial and continuing board certification and other related topics. He also led the development and validation of a novel objective structured clinical examination that was incorporated into the initial certification process for anesthesiologists, the first such examination among member boards of the American Board of Medical Specialties (Chicago, Illinois). Finally, he published seminal work examining substance

use disorder among anesthesiologists, showing that despite ongoing educational and support efforts, this problem continues to grow.

Research Education and Mentorship

Dr. Warner also inspires others to pursue research careers. He has mentored more than 40 graduate students and research fellows, as well as numerous junior faculty, with several subsequently establishing their own independent National Institutes of Health–funded research programs. His understanding of study design and research methods is extraordinary, as is his ability to teach this material to novice researchers. As a scientist, he has the rare gift of making complex, difficult concepts clear and easy to understand. His gentle and unassuming manner makes him easily approachable, and thus, when combined with his research expertise, he is the very model of a professor.

He is also an active educator in all five schools of the Mayo Clinic College of Medicine and Science and has received numerous awards for excellence in teaching. He founded and leads the College's Office for Applied Scholarship and Education Science, which brings the expertise of professional educators to Mayo Clinic educational programs, and is currently an Associate Dean for Faculty Affairs in the Mayo Clinic Alix College of Medicine.

Leadership and Services Roles in Research

Dr. Warner's commitment to promoting research is also apparent in his numerous leadership roles in institutional research administration in addition to his past role as Vice-Chair for Research in our Department of Anesthesiology and Perioperative Medicine. Research at Mayo Clinic is managed by a central institutional research committee. Dr. Warner has served in many different capacities on this committee and its subcommittees, including as Associate Dean for Clinical and Translational Research, Co-Director of the Office for Diversity in Clinical Research, Co-Principal Investigator and Associate Director of the Mayo Clinic Center for Clinical and Translational Sciences (CTSA award), and Principal Investigator of its associated KL2 Mentored Career Development award. Remarkably for an anesthesiologist, he also led for many years the institution's efforts to support community-engaged research. Thus, while maintaining his own active research program, he also has been and remains a major leader in clinical research throughout the institution, amplifying his influence.

Dr. Warner has also made other significant contributions to our specialty. For example, he served full terms as both Associate and Full Editor for the journal Anesthesiology. He has served as an *ad hoc* member for numerous National Institutes of Health study sections and chaired the ASA Subcommittee on Respiration for several years. He was recognized for his research excellence by being selected to give the Helrich Memorial Lecture by the Foundation for Anesthesia Education and Research.

Clinical Activities

It is remarkable that Dr. Warner has been able to accomplish all this while maintaining an active clinical practice. He was a founding member of our department's Pediatric Anesthesia Division, introduced nitric oxide into clinical practice at Mayo Clinic, and is recognized by his peers as a skilled and compassionate clinician. He has also been active in medical missions to underserved countries.

Summary

The breadth and quality of Dr. Warner's scientific accomplishments are remarkable. The methods used in his research range from saturation transfer difference nuclear magnetic resonance spectroscopy examining anesthetic binding to isolated proteins to cutaneous blood flow measurements in humans to randomized clinical trials of tobacco interventions to education science assessments to the tools of dissemination and implementation research in clinical anesthesiology practices, showing that sound scientific principles can be applied to any area of inquiry with success—if the investigator has curiosity and drive. He is the very model of the physician–scientist yet has not followed a "safe," traditional career path. Many scientists maintain their funding stream by developing an ever-more specialized expertise in a relatively narrow area that is recognized and rewarded by peer reviewers. In contrast, Dr. Warner has, when appropriate, completely changed scientific direction to pursue his passions while still maintaining scientific excellence and productivity. Along the way, he continues to recruit and train the best and brightest in scholarly anesthesiology careers. Dr. Warner has made extraordinary contributions to our specialty in multiple domains that will benefit our patients and is truly deserving of recognition for these efforts. Despite these scientific accomplishments, if you ask him, his greatest joys are Julie, his high school sweetheart and wife of 43 yr, his three grown-up children and five (so far) cute grandchildren.

Competing Interests

Dr. M.A. Warner is a first cousin of Dr. D. O. Warner, and both are members of the Mayo Clinic (Rochester, Minnesota) Department of Anesthesiology and Perioperative Medicine.

Correspondence

Address correspondence to Dr. Warner: Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905. warner.mark@mayo.edu