Anesthesiology 2005; 103:684–6

David S. Warner, M.D.

Recipient of the 2005 Excellence in Research Award

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THE winner of the 2005 American Society of Anesthesiologists Excellence in Research Award is David S. Warner, M.D., Professor of Anesthesiology, Neurobiology, and Surgery at Duke University Medical Center, Durham, North Carolina. Although Dr. Warner's achievements are internationally recognized across a broad spectrum of highly competitive fields such as neurobiology, neurology, neuroanesthesiology, stroke physiology, and biochemistry, ironically, his contributions to these areas may be "off the radar screen" for some practicing anesthesiologists. Perhaps this is because Dr. Warner is an individual with quiet dignity, one who does not need to trumpet his accomplishments. The quality of Dr. Warner's scientific accomplishments speak for themselves and have changed medicine.

David Warner is a Midwesterner, born, raised, and educated in the heartland of the United States. Born in Evanston, Illinois, on July 20, 1953, David was raised in Oshkosh, Wisconsin, and completed college with a B.A. degree in psychology from the University of Wisconsin, Madison, Wisconsin, in 1976. His first scientific article resulted from a senior research project investigating interactions between acoustic and auditory perception. David stayed in Wisconsin for medical school, graduating from the University of Wisconsin-Madison with the M.D. degree in 1980. He then moved to another part of the Midwest, The University of Iowa, Iowa City, Iowa, to pursue an interest in clinical neuroscience as a neurosurgery resident. During a required anesthesia rotation in his surgery residency, David realized that his true passion in medicine was anesthesia, so he switched careers to start an anesthesiology residency at The University of Iowa and never looked back. Because of his background in psychology and neurosurgery, not surprisingly, David found his clinical base in neuroanesthesiology. Soon after completion of his anesthesiology residency in 1984, to pursue further training in basic mechanisms underlying neuroprotection, David moved to Sweden to spend a year in the Laboratory of Experimental Brain Research at the University of Lund. His mentor, Bo K. Siesjö, M.D, Ph.D., offered him exposure to world-class neuroscience in the study of pathologic brain energy metabolism. David then returned to the faculty in the Department of Anesthesia at The University of Iowa, where he worked closely with Michael M. Todd, M.D., from 1987 to 1994 under the leadership of department chair John H. Tinker, M.D. Initially supported by the Foundation for Anesthesia Education and Research, David rapidly developed his own National Institutes of Health (NIH)–funded line of scientific investigation, continued fruitful collaborations with Mike Todd, and administered the University of Iowa Anesthesiology research training grant. In 1992, David became director of the Division of Neuroanesthesiology in the Department of Anesthesia at The University of Iowa College of Medicine, a testament to his clinical and teaching skills in addition to research prowess. In February 1994, Dr. Warner moved his laboratory and some of his staff to Durham, North Carolina, where he become Professor of Anesthesiology, Neurobiology, and Surgery in the Department of Anesthesiology at Duke University Medical Center and is currently Vice-Chairman for Academic Development and Director of the Multidisciplinary Neuroprotection Laboratories.

Dr. Warner is one of the world's most respected neuroanesthesiologists, whether viewed from inside anesthesiology or "outside" from neurology, physiology, or biochemistry perspectives. With his focus on mechanisms of stroke and brain protection, Dr. Warner is often the speaker of choice at international meetings on brain protection; in fact, some international societies have chosen their meeting dates around Dr. Warner's availability. Taking after his mentor, Mike Todd, David has built multidisciplinary teams of investigators across fields such as anesthesiology, neurology, biochemistry, neuroradiology, pediatrics, neurosurgery, cell biology, and neurobiology. He asks probing questions, and then uses a range of tools at the cutting edge of medical research to answer these questions. As a result, his publications use a range of approaches, including rat and transgenic mouse outcome models of central nervous system (CNS) injury, hippocampal slices, tissue culture, magnetic resonance imaging, and biochemical and genetic analyses. He is frequently called upon by investigators from many disciplines to perform sophisticated protocols of neurologic injury analysis on their transgenic/knockout mice. David has successfully recruited outstanding scientists from all over the world to synergize in creating a unique neuroscience brain protection group covering almost an entire floor of one of the research buildings in Duke University Medical Center; this group now includes six principle investigators exemplified by a neuroradiologist who runs an on-site animal magnetic resonance imaging facility, a biochemist focusing on endoplasmic reticulum responses to brain injury, neurologists and anesthesiologists using vari-

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Submitted for publication August 4, 2005. Accepted for publication August 4, 2005.

ous animal models to explore acute CNS injury, a pediatric anesthesiologist exploring mechanisms of fetal brain injury, and David's own group, focusing on mechanisms of neuroprotection by anesthetics and antioxidants. Dr. Warner has been consistently funded by the NIH (multiple R01 grants) during his entire career and has served on NIH (National Institute of General Medical Science–sponsored) study sections focused on evaluating pharmacology and anesthesiology training grants. In addition to his major laboratory efforts, clinically, David has been instrumental in the safe introduction of several drugs into neuroanesthesia practice and has served as the Physician Protocol Monitor for the NIH-funded multinational Intraoperative Hypothermia for Aneurysm Surgery Trial. In the laboratory, his work has focused primarily on development of valid rodent (rat and mouse) outcome models of brain and spinal cord ischemia/trauma, perinatal hypoxia–ischemia, and subarachnoid hemorrhage. His most significant contributions relate to effects of anesthetic agents on outcome from these injuries, genomic contributions to ischemic/traumatic outcome, role of hyperglycemia in ischemic brain injury, contribution of extracellular reactive oxygen species to neural tissue demise, and mechanisms of cerebral vasospasm. These studies are briefly described below.

One can divide David's research career into two periods: The University of Iowa period and the Duke University period. In his initial career in Iowa, David's key findings included identifying unique patterns of cerebral blood flow distribution for different anesthetic agents and interrelationships with metabolic rate,[1–4] effects of anesthetics on patient responses to craniotomy,[5,6] identification of *N*-methyl-D-aspartate receptor glycine recognition site as a valid target for ischemic neuroprotection,[7–9] identification of the importance of osmotic pressure in defining effects of intravenous volume expanders on brain water content in models of CNS injury,[10–13] defining additive interactions of ester–ester and ester–amide local anesthetic combinations in producing CNS toxicity,[14] and discovering efficacy of insulin in reducing diabetes-induced hyperglycemia-augmented ischemic brain injury.[15] Also during this period, David performed an elegant set of experiments introducing comparison of anesthetics to the awake state (rather than an alternative anesthetic state) when assessing for neuroprotection.[16,17] These studies provided a more appropriate frame of reference in discerning drug efficacy and also introduced the importance of brain temperature regulation in defining efficacy of anesthetics. During the next (Duke) phase of David's career, key findings to date have included defining the importance of apolipoprotein E alleles in outcome from CNS injury, including influences on oxidative stress and neuroinflammation,[18–21] identifying major neuroprotection by volatile anesthetics against global cerebral ischemia independent of effects on systemic stress,[22,23] identifying the γ-aminobutyric acid type A receptor as a prominent site of volatile anesthetic action in providing ischemic neuroprotection,[24] discovering that extracellular superoxide dismutase is a critical factor in defining outcome from acute CNS injury,[25–27] identifying delayed and profound neuroprotection from metalloporphyrin catalytic antioxidants,[28–30] leading introduction of remifentanil into neuroanesthesia practice,[31–33] defining the role of P50 in hypothermic neuroprotection,[34] inventing and advancing models of CNS injury in mice allowing study of transgenic strains,[35–37] defining postoperative nausea and vomiting epidemiology and treatment efficacy in patients undergoing craniotomy,[38–40] and discovering efficacy of β-hydroxy-β-methylglutaryl-CoA reductase inhibitors (statins) in treatment of subarachnoid hemorrhage-induced cerebral vasospasm.[41,42] Dr. Warner has published more than 180 original manuscripts in prestigious journals such as *Neuroscience*, *Journal of Neuroscience*, *Journal of Biology and Chemistry*, *Stroke*, *Journal of Cerebral Blood Flow Metabolism*, ANESTHESIOLOGY, *Anesthesia & Analgesia*, *Critical Care Medicine*, *Annals of Neurology*, *Neurosurgery*, and *Journal of Neurosurgery*.

In addition to research, David has also played a major role in research training and fellow/faculty development. He is principal investigator on Duke's NIH-funded institutional research training grant, having written the original grant and successfully leading several competitive renewals. In his own laboratory, more than 60 individuals have been trained, ranging from high school students to postdoctoral research fellows, with about a 50–50 balance between American citizens and international fellows. More than 80% of these trainees remain in academic practice. Many have established their own laboratories in the United States, Europe, and Asia and have obtained competitive peer-reviewed funding to support their ongoing work. Many have been supported in their training by competitive funding mechanisms (Foundation for Anesthesia Education and Research, International Anesthesia Research Society, American Heart Association, NIH) and have won national or international prizes for their research. Dr. Warner also serves as the Vice-Chair for Academic Development in a department of 75 faculty members, having specific responsibilities for programmatic academic development of junior faculty. He can often be found late at night reviewing fellow and junior faculty grant applications; no one is more dedicated to the training of future academicians in our specialty than David. In addition to his research advancements, Dr. Warner's career and responsibilities in the anesthesiology community are exemplary. He is a past president of the Society for Neurosurgical Anesthesia and Critical Care. Dr. Warner has been a very active and dedicated section editor for *Anesthesia & Analgesia*, organizing experts to review articles from a cross-section of anesthesiology as well as having particular emphasis on reviewing neuroscience studies. He is also on numerous other editorial boards including *Journal of Anesthesia*, *Neurocritical Care*, *Journal of Neurosurgical Anesthesia*, and ANESTHESIOLOGY. Many have benefited from Dr. Warner's thoughtful review of their research manuscripts and grants,

through his insightful comments and his ability to hone in quickly on key strengths and weaknesses. David has also served as an American Board of Anesthesiology oral board examiner.

In spite of his notoriety and recognition, Dr. Warner is a very down-to-earth teacher and researcher and a warm human being. He guides residents through anesthesia for craniotomy surgery and teaches the essentials of safe human neuroanesthesiology. He leads by example in his research laboratory, working harder than his research fellows. He consistently helps fellows learn to write clear and cogent research manuscripts and grants. No one is a more passionate believer in the academic enterprise. Dr. Warner's work with research trainees in their career development stems from his strong belief that physician–scientists are critical in integrating basic science and clinical medicine. He is certainly deserving of the 2005 American Society of Anesthesiologists Excellence in Research Award.

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