SPECIAL ANNOUNCEMENT

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Gary Strichartz: Life Among Local Anesthetics

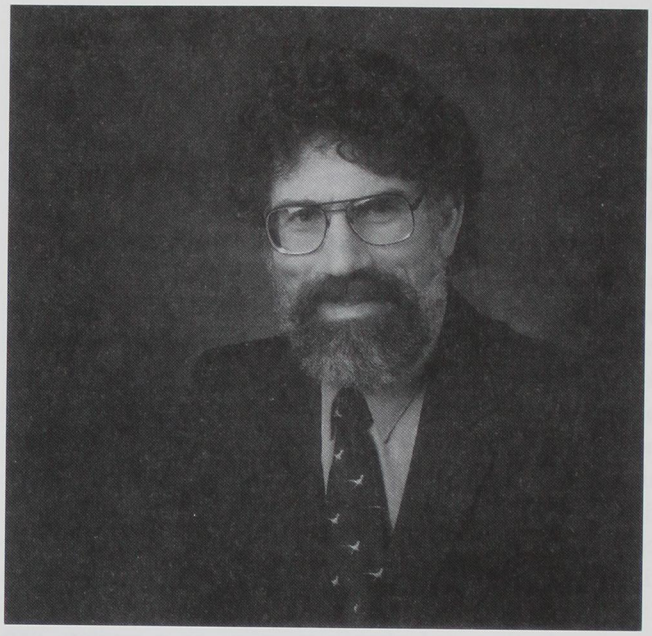
Recipient of 1998 Excellence in Research Award

THE American Society of Anesthesiologists (ASA) Excellence in Research Award is presented in 1998 to Dr. Gary Strichartz, Professor of Anaesthesia and Pharmacology at Harvard Medical School and Vice-Chair for Research in the Anesthesia Department at Brigham and Women's Hospital. Dr. Strichartz is recognized by this award for his outstanding contributions to our knowledge of local anesthetics over the past 25 years, influencing the fundamental views on this subject that are held by basic scientists and clinical anesthesiologists.

Born and reared in Washington, D.C., Dr. Strichartz graduated from Antioch College with a B.S. in Physics and from the University of Pennsylvania with a Ph.D. in Biophysics. Although his doctoral research, conducted under Professor Britton Chance, concerned light-driven changes in photosynthetic pigments, it was in graduate school that he first developed an interest in psychopharmacology. In 1970, little was known about ion channels of nerve or any other membranes. Dr. Strichartz journeyed to Seattle to study with Bertil Hille, then a new faculty member at the University of Washington. His serendipitous discovery of "use-dependent" block by local anesthetics while a postdoctoral fellow in Hille's lab was a premonition of his later involvement in anesthesia research.

After spending the summer of 1972 as a Grass Fellow with Dr. Clay Armstrong at the Marine Biological Laboratory at Woods Hole, Dr. Strichartz became a senior postdoctoral fellow with Professor J. M. Ritchie at Yale University. There he began the research on biotoxins that has complemented his investigations of ion channel pharmacology. Together with Ritchie, Richard Henderson (now head of the MRC laboratories in Cambridge, U.K.), and Richard Rogart, he extended methods for radiolabeling toxins and understanding the energetics of their interactions with Na^+ channels.

In 1975, Dr. Strichartz took a faculty position in Physiology and Biophysics at State University of New York, Stony Brook, departing there in 1981 to become Associate Professor of Pharmacology (in Anesthesia) at Harvard Medical School. This move was in response to an invitation from then newly appointed Professor of Anaesthesia at the Brigham and Women's Hospital, Benjamin Covino. Working together with clinical colleagues and researchers recruited from Dr. Covino's original group at Astra Pharmaceuticals, they built one of the preeminent groups studying local and regional anesthesia. Today these research laboratories are a magnet attracting visitors and fellows interested in local anesthetics from all over the world.



Professor Gary Strichartz, Ph.D.

Dr. Strichartz's research on local anesthetics falls into three areas. He showed through the original observation and analysis of "use-dependent" inhibition that the sodium channel was the actual receptor for local anesthetics during impulse blockade. This work also provided a basis for understanding the cardiotherapeutic mechanism of class I antiarrhythmic drugs. In later work he and his colleagues showed how the physical-chemical prop-

erties of local anesthetics, which his group has systemically characterized, could explain their affinities and binding rate constants for sodium channels and how the different states of the channels contributed to overall "use-dependence." Past and present work with stereoisomers of local anesthetics led to the novel idea of two anesthetic binding sites on the Na^+ channel. His more recent research into general mechanisms compares the pharmacology of local anesthetic inhibition of K^+ and Ca^{2+} channels with that of Na^+ channels, in a search for common motifs and sites of action among these structurally similar channels. At present he is investigating the potent actions of local anesthetics on G-protein–coupled receptors. These surprising effects probably play an important role in spinal and epidural anesthesia and may also contribute to central nervous system and cardiovascular toxicity.

During the past 5 years Dr. Strichartz's laboratory has begun work to better understand clinical local anesthesia. They have developed a sophisticated model for peripheral block, using the rat sciatic nerve, in a combination of multifunctional behavioral testing, *in vivo* neurophysiology of single sensory fibers, and measurements of local anesthetic uptake by nerve. This approach has been applied to two areas relevant to clinical anesthesia, showing (1) that the reduction in local anesthetic requirement during pregnancy results from pharmacodynamic rather than pharmacokinetic changes, and (2) that the acute tolerance (tachyphylaxis) for local anesthetic action that follows repeated cutaneous or peripheral nerve block has a pharmacokinetic basis. Both of these findings should reform the practice of local anesthesia and stimulate related clinical studies.

Dr. Strichartz's research extends beyond local anesthetics. He is well regarded for his original studies on the pharmacology of saxitoxin and tetrodotoxin acting on Na^+ channels. These investigations included the development of a high specific radiolabeled saxitoxin, which he used to study the molecular properties and the development and growth-associated changes of sodium channels and which many others used for the original isolation and purification of sodium channels. Recently he and colleagues have focused on the application of these toxins for nerve blocks *in vivo,* with promising results for long duration blockade.

The toxin research has also led to the isolation, purification, and biochemical and physiologic characterization of a number of peptide toxins from the venom of scorpions and cone snails. These toxins act on Na^+, K^+, and, uniquely, Cl^- channels of cellular membranes and are being further developed into useful diagnostic and therapeutic tools.

Five years ago, Dr. Strichartz expanded his core interest in local anesthetics to the larger arena of pain. Supported by an expansion of the anesthesia department's research and related growth at the Brigham and Women's Hospital, he founded a Pain Research Center with interdisciplinary laboratories studying acute and chronic pain and using methods ranging from molecular biology to neurobehavior and from ion channel pharmacology to whole animal toxicology. The present themes of this group are the understanding of and development of therapeutics for postoperative pain as well as chronic neuropathic pain from peripheral nerve origins. Not surprisingly, local anesthetics are agents of interest in many of these investigations.

Dr. Strichartz has been continuously funded by the National Institutes of Health (NIH) since 1976 and also has received grants from the Multiple Sclerosis Society, mentored postdoctoral Fellows funded by the Muscular Dystrophy Association and by local chapters of the American Heart Association, and been substantially supported by several industrial sources. He has served as an *ad hoc* reviewer for NIH, National Science Foundation, and the Veterans Administration Merit Program. His research is recognized internationally. He was the first non-anesthesiologist to be named the visiting Stuart Cullen Professor at the University of California, San Francisco's Anesthesiology Department and the first nonphysician Ph.D. to be appointed to the Editorial Board of ANESTHESIOLOGY. From his position on that board, he initiated the present-day journal-sponsored symposia for the ASA annual meeting, and he has personally organized or coorganized five of the seven symposia since their inception. His duties for ASA also include 6 years service on the Research Committee, with a similar role for 2 years for the American Society for Regional Anesthesia. Professor Strichartz also serves on the editorial boards of *Regional Anesthesia* and *Toxicon* and was previously an Associate Editor of *Neuroscience Letters.*

Teaching is an active part of Dr. Strichartz's professional life, both for courses at national and international meetings and for lectures at home. He is highly regarded for his ability to clarify complex scientific areas for clinical audiences. At Harvard Medical School he is one of the most popular lecturers in a highly rated pharmacol-

ogy course, and he enjoys the same standing for his part in the MIT Health Science and Technology Program's medical pharmacology block. He has mentored more than 15 postdoctoral fellows, both Ph.D.s and M.D.s, and 5 doctoral students have completed dissertations under him, in disciplines as diverse as cell and developmental biology, pharmacology, and biophysics.

At this time when the use of and interest in local anesthetics is expanding rapidly, it seems worthy to recognize the activities of one of the leaders in this field and of one of the generous contributors to our specialty and this Society.

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