

# AES News

AMERICAN EPILEPSY SOCIETY

Vol. 11, No. 1

Winter 2002

## Recent Advances in Epilepsy Research

Katherine D. Holland, M.D., Ph.D., Cleveland Clinic

The National Institute of Neurological Disorders and Stroke (NINDS) recently published future directions for epilepsy research which moves from controlling the symptoms of epilepsy (seizures) towards a search for a cure.<sup>1</sup> This initiative includes wide ranging guidelines with a unified goal of preventing epilepsy in patients who are at risk for developing this disorder and for the complete cessation of seizure activity without side effects in those who are already affected. Research will be aimed at understanding the basic anatomical, physiological and molecular substrates of epileptogenesis by developing and studying animal models of epileptogenesis and epilepsy. These models will be used to identify markers of epileptogenesis and to test novel therapies. It is hoped that this will lead to clinical trials of potential anti-epileptogenic agents in people who are at risk for developing epilepsy.

For those who are already affected, the initiative includes goals to create therapies that are free of medication side effects. Strategies such as the application of pharmacogenomic approaches to identify patients who are likely to respond to therapies or are at risk for side effects will be encouraged. Alternative treatment strategies include the identification and modulation of diffuse neuronal systems that may be involved in multifocal or symptomatic generalized epilepsy, and use of focal treatments such as microstimulators, localized drug delivery systems or cell transplantation. Some of these approaches will require the development of sensors to detect sei-

zures before the onset of clinical symptoms. Finally, the initiative also encourages the development of improved neuroimaging to identify and localize the cause of seizures in patients with cryptogenic seizures and to better determine the extent of the epileptogenic zone in symptomatic epilepsy. Investigators are already addressing many of the research directions outlined by the NINDS.

### Mechanisms of Epileptogenesis

The contribution of seizures to epileptogenesis is a controversial topic. Kindling occurs in certain animal models of epilepsy. However, the notion that seizures produce brain damage in humans and as a result contribute to epilepsy has been a subject of debate. Understanding the conditions that lead to epileptogenesis in humans is important to the prevention of epilepsy. Several

*Continued on page 9*

### PRESIDENT'S MESSAGE



Three months ago, AES gathered in Philadelphia for our annual meeting. Although some organizations canceled conferences or saw attendance sharply down after the

September 11 events, we had a solidly successful meeting. Attendee numbers held steady; enthusiasm was unabated. This indication of AES members' commitment and of the importance of the meeting is only one of many reasons I am honored to be serving as your new president.

This year I intend to build on the momentum of prior presidents and boards as we move ahead with the long range planning process. This effort will involve the entire AES leadership and committee chairs as well as the general membership. Long range planning is an ongoing process in AES; we periodically review progress on previous goals, formulate new ones and revisit our mission: *AES promotes research and education for professionals dedicated to the prevention, treatment and cure of epilepsy.*

In 1997, the Society set three major strategic goals. There has been significant progress in reaching milestones for each of these goals. The first goal called for AES to be its members' primary resource for scientific and clinical education and knowledge exchange about epilepsy. Under the direction of Mike Rogawski and the Technology Committee, our web site at [www.aesnet.org](http://www.aesnet.org) has been revamped into a powerful source for information and networking. Last year also saw the launch of the AES online and print review journal *Epilepsy Currents*, thanks to Susan Spencer, Bob Macdonald and their bevy of editors. And we have seen that the AES Annual Meeting continues to be our premier educational venue. These major new resources have substantially con-

*Continued on page 2*

### INSIDE THIS ISSUE

AES Members Join Board, Nominating Committee .....	3
<b>EF Update</b> /Legislative News .....	4
Resource For Genetics Research .....	4
<b>NINDS Report</b> /Stem Cell Registry .....	5
<b>Practice Rx</b> /AED Shortages .....	5
Highlights of the 2001 Joint Meeting .....	6
<b>AES Conversation With</b> / Steven J. Rugens, CMP .....	8
<b>AES Circuit</b> /New Navigation .....	8
Communicate Electronically With AES ...	11
Calendar of Events .....	11



# AES News

AES News is published by the American Epilepsy Society, American Branch, International League Against Epilepsy.

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Membership consists of clinicians, scientists investigating basic and clinical aspects of epilepsy, and other professionals interested in seizure disorders. Members represent both pediatric and adult aspects of epilepsy. Active membership for one year is \$170 and includes a subscription to the journal *Epilepsia*. Junior Membership is \$130 annually; *Epilepsia* subscription is optional for Junior members. Active and Junior membership is limited to residents of the USA, Canada, and Mexico. Corresponding membership is limited to residents outside of North America. It does not include a subscription to *Epilepsia*, and fees are \$125. Senior membership is available to Active Members who have reached the age of 65.

**Editorial Deadlines**

Summer 2002 issue: May 6, 2002  
Fall 2002 issue: August 30, 2002  
Winter 2003 issue: January 24, 2003

## President's Message

(continued from page 1)

tributed to making the AES a source of information on a wide range of issues and topics for its members.

Our second strategic goal was for AES to be a recognized advocate and resource for scientific

research in the prevention, treatment and cure of epilepsy. Outgoing Research and Training Committee chair Bob Macdonald's efforts on strengthening and promoting an effective Research and Training Committee to develop and manage research funding sources have been quite fruitful. In partnership with the Epilepsy Foundation, the Milken Family Foundation, CURE and others, AES has made significant contributions to epilepsy research efforts at the pre- and post-doctoral levels. John Swann, who also chairs the EF research grants subcommittee, will be assuming leadership of the AES R&T Committee. This dual role will ensure close coordination with other research programs seeking to advance the understanding of epilepsy and its therapeutics.

Immediate past president Nico Moshé has been very effective in advancing our goal for AES to be the leader in developing resources and collaborative relationships worldwide to advance patient care, as well as to support efforts leading to the prevention and cure of epilepsy. AES entered into mutually beneficial arrangements with other "interested parties" in epilepsy, such as AAN's One Voice Initiative and ILAE. These partnerships help leverage the Society's influence; as we move ahead on long range planning, looking outward to the larger epilepsy community will help us put the resources of AES and its members squarely behind a range of advocacy efforts crucial to preventing, treating and curing epilepsy. Initiatives to develop an external communications strategy have shown that this will be a long term process, but it is essential to ensuring that the Society has an influential voice to transmit our expertise and talent on behalf of people with epilepsy.

This also is the time for strengthening the Society's infrastructure. Several years ago, Bob Macdonald oversaw a reconfiguration of AES committees and instituted procedures to bring more people onto committees

*This year I intend to build on the momentum of prior presidents and boards as we move ahead with the long range planning process.*

by matching member interest to Society needs. We continue to try to annually place as many volunteers as possible on AES committees. With that process in place, we will be turning our attention this year to developing a board culture that focuses on advancing strategic goals by exercising stewardship promoting the effectiveness of our committees.

Lately there has been increasing new information supporting the view that seizures have disruptive consequences far beyond those overtly symptomatic seconds or minutes of the usual ictal event. This year I will convene a task force to study how AES should address and respond to the growing evidence about adverse consequences of epilepsy, and how to make that information available to various advocate organizations. This important topic will also be the topic of this year's Presidential Symposium.

I began this message by talking about the AES Annual Meeting, an event that has grown from a few hundred attendees to nearly 3,000 over the past 15 years. The meeting is the AES centerpiece, and in this year of strategic planning we have an excellent opportunity to review the meeting's length, content, timing and member needs. During this year the past, current, and next chairs of key meeting components (such as the Scientific Program, Annual Course and Investigators' Workshop) will convene to discuss the options and possibilities for future directions of the AES Annual Meeting. This will likely be the start of an evolving process during the next few years on this most important of annual AES activities.

Thank you for your continued support of the AES and its leadership. It is a pleasure to work with you on behalf of people with epilepsy, and I am determined to build on the past successes of the AES and its members to promote the prevention, treatment, and cure of epilepsy.

Thomas P. Sutula, M.D., Ph.D.

# AES Members Join Board, Nominating Committee

Four AES members have assumed new leadership positions within the Society. Daniel H. Lowenstein, M.D. was elected AES Second Vice President; Jaideep Kapur, M.D., Ph.D. and John M. Pellock, M.D. have joined the AES Board of Directors; and John W. Swann, Ph.D. became a member of the Nominating Committee. Susan Spencer, M.D. chaired the Nominating Committee that prepared the 2001 slate for the membership vote. Installation of the elected nominees took place during the AES Annual Business Meeting in Philadelphia in December 2001.

Profiles of these four ASE members follow, along with a listing of the complete AES Board of Directors.

## Second Vice President

### *Daniel H. Lowenstein, M.D.*



Dr. Lowenstein is the Carl W. Walter Professor of Neurology and Dean for Medical Education at Harvard Medical School, and Director of the Program in Brain Plasticity and Epileptogenesis in the Department of Neurology at the Beth Israel Deaconess Medical Center. He received his M.D. from Harvard and neurology training at UCSF. After completing a fellowship in molecular biology, he joined the UCSF faculty and established the UCSF Epilepsy Research Laboratory before moving to Harvard. His research has focused on fundamental mechanisms of neuronal network remodeling that occur during epileptogenesis, and the management and treatment of patients with status epilepticus.

Dr. Lowenstein currently chairs the AES Education Council and the Merritt-Putnam Symposium, and is a member of the NINDS Advisory Council. He received an AES/Milken Family Foundation Epilepsy Research Award in 2001.

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## Board of Directors

### *Jaideep Kapur, M.D., Ph.D.*



Dr. Kapur is an Associate Professor in the Department of Neurology at the University of Virginia. He received his M.D. from the University of Delhi, India; and his Ph.D. in Neuroscience from the University of Virginia. Dr. Kapur completed a neurology residency at

the Medical College of Virginia and an epilepsy and neurophysiology fellowship at the University of Michigan, where he was also a faculty member. His research has focused on the cellular mechanisms of status epilepticus.

Dr. Kapur has received the AES Junior Investigator Award and the William G. Lennox fellowship. A member of the Professional Advisory Board of the Epilepsy Foundation, he serves also as an editor of both *Epilepsy Research* and *Epilepsy Currents*. He is a current member of the AES Continuing Medical Education Committee.

### *John M. Pellock, M.D.*



Dr. Pellock is Chairman, Division of Child Neurology and Vice Chairman, Department of Neurology at the Medical College of Virginia, Virginia Commonwealth University, where he

is also Director of the Comprehensive Epilepsy Institute and Professor of Neurology, Pediatrics, and Pharmacy and Pharmaceuticals. He received his M.D. from Saint Louis University and pediatrics training at the Medical College of Virginia, and completed a fellowship in child neurology at Columbia-Presbyterian Medical Center. He has published and lectured extensively on pediatric epilepsy, as well as conducting clinical research in antiepileptic drug development and therapy.

Dr. Pellock has served on a variety of AES committees and currently co-chairs the Corporate Advisory Committee, AET Symposium and Children's Hour. As Director of the International Epilepsy Consortium, he works with AES to provide guidance to young clinical investigators.

## Nominating Committee

### *John W. Swann, Ph.D.*



Dr. Swann is a Professor in the Department of Pediatrics and Division of Neuroscience at Baylor College of Medicine and Scientific Director of The Gordon and Mary Cain Pediatric Neurology Research Foundation Laboratories at Texas Children's Hospital. He received his Ph.D. from the University of Maryland, with postdoctoral training at the National Naval Medical Center and University of Goteborg in Sweden. Dr. Swann's research

has focused on understanding the basic processes that underlie epileptogenesis in the developing hippocampus.

Recipient of a Javits Neuroscience Investigator Award and an AES/Milken Family Foundation Epilepsy Research Award, Dr. Swann has served on the AES Board, chaired the Investigators' Workshop Committee, and been a member of the Awards Committee and Research Funds Committee. He is as well a current member of the Professional Advisory Board of the Epilepsy Foundation.

## AES 2002 Board of Directors

### *President*

Thomas P. Sutula, M.D., Ph.D.

### *First Vice President*

Jeffrey L. Noebels, M.D., Ph.D.

### *Second Vice President*

Daniel H. Lowenstein, M.D.

### *Treasurer*

Ruben I. Kuzniecky, M.D.  
(2000-2002)

### *Assistant Treasurer*

Steven C. Schachter, M.D.  
(2002)

### *Past President*

Solomon L. Moshé, M.D.

### *Board Members*

Joan K. Austin, D.N.S., RN  
(2000-2002)

F. Edward Dudek, Ph.D.  
(2001-2003)

Jaideep Kapur, M.D.  
(2002-2004)

Jacqueline A. French, M.D.  
(2000-2002)

John Pellock, M.D.  
(2002-2004)

Michael A. Rogawski, M.D., Ph.D.  
(2001-2003)

### *Ex Officio*

Cesare T. Lombroso, M.D., Ph.D.

Robert S. Fisher, M.D., Ph.D.

# Federal Appropriations Bring Good News

Ann Scherer, *Epilepsy Foundation*

The 2001 budgeting season in Washington, D.C. ended with good news from Congress on key legislative issues of importance to the research community and to people with epilepsy and their families.

Appropriations for the National Institute of Neurological Disorders and Stroke (NINDS) and the epilepsy program at the Centers for Disease Control and Prevention (CDC) were increased, and, in the case of the NINDS appropriation, the report language specifically called for increased attention to epilepsy research.

The new National Institutes of Health budget will include \$1.3 billion for NINDS and \$6.5 million for the epilepsy program at the CDC.

The CDC figure represents a 59 percent increase over the previous year, which is particularly impressive, given that overall funding for chronic disease is about comparable with last year. In fact, in reconciling the higher appropriations proposed by the House with the lower Senate numbers, the conferees generally split the difference in almost every area *except* for the epilepsy program, which retained the higher House number.

The increasing success of the Foundation's advocacy on behalf of epilepsy research and the CDC epilepsy programs is due to the work of volunteers and staff in our Speak Up Speak Out Campaign, who worked throughout the year to ensure legislators were aware of the critical need to expand epilepsy programs, and in particular those who attended the Public Policy Institute last spring and made personal Congressional visits.

Preparations are now under way for the March, 2002 Public Policy Institute (PPI) which, as in previous years, is receiving support from the American Epilepsy Society and from Pfizer, Inc. The Institute provides training to grassroots advocates and affiliates in the skills necessary to make the case for epilepsy-related research and support on Capitol Hill.

This year will see the debut of a new form of grassroots advocacy – the Kids Speak Up program, which will bring thirty children with epilepsy and their parents to Washington, D.C. to join with PPI participants for training

and Hill visits. Kids Speak Up is supported by a grant from Abbott Laboratories.

Report language in the Labor, Health and Human Services bill not only urged NINDS to pursue promising leads in epilepsy research, but also called on the agency to establish an annual lectureship “to provide the intellectual stimulation to prompt new findings in both the NINDS intramural program and the extramural community.”

The report further asked NINDS to consider naming the lectureship in memory of Judith Hoyer, wife of Rep. Steny Hoyer (D-MD). Mrs. Hoyer, who had epilepsy, spent her life helping families dealing with the condition and promoting research into a cure and a better quality of life for those with epilepsy. A strong supporter of epilepsy-related issues on Capitol Hill, Mrs. Hoyer was also a member of the Epilepsy Foundation's board of directors.

## \*NSYNC Clicked with Teens

The theme for the November, 2001 Epilepsy Month focused on teens and their experiences at school. \*NSYNC, the sensationally popular band, helped carry the message that

teens with epilepsy — like everyone else — are Entitled to Respect.

Early tracking data suggest that the message reached thousands of young people. More than 59,500 visited the Entitled to Respect section of the Foundation's new BLURT site for teens; the group's radio message endorsing respect for kids with seizures received more than 10,000 plays on radio stations popular with teenagers; and affiliates distributed 90,000 copies of the Entitled to Respect brochure to schools and similar venues.

Visits to the [www.efa.org](http://www.efa.org) website during November (Epilepsy Month) reached a record 132,000 – 35 percent higher than the usual monthly average. Total visits to the teen and regular site amounted to more than 191,000, double that of the previous year. Both video and audio news releases about the campaign were played throughout the country.

The \*NSYNC participation was made possible by a grant from Abbott Laboratories. Other aspects of the Entitled to Respect campaign were supported by the CDC.

## Resource For Genetics Research Gene Discovery Project

The Epilepsy Foundation invites applications from scientists who wish to gain access to the pedigree information entered into the Foundation's Gene Discovery Project relational database.

The Epilepsy Foundation, via its website, is collecting data on a voluntary and confidential basis from people who have a family history of epilepsy. Approved researchers are granted access to query the database and select pedigrees that match their genetic studies. The Epilepsy Foundation will serve to introduce researchers to families they may wish to invite to participate in a specific study.

More information about the Gene Discovery Project can be found by visiting [www.epilepsyfoundation.org/gene/](http://www.epilepsyfoundation.org/gene/).

Inquiries are invited from researchers who meet all the eligibility criteria outlined in the application. All research must be conducted within the United States.

Applications are accepted on a rolling basis throughout the year. Applications can be found at [www.epilepsyfoundation.org/GDPApplication](http://www.epilepsyfoundation.org/GDPApplication), or contact:

Epilepsy Foundation, Gene Discovery Project, 4351 Garden City Drive, Landover, MD 20785-2267. Phone: (301) 459-3700; fax: (301) 577-2684; e-mail: [grants@efa.org](mailto:grants@efa.org)



## NINDS REPORT

# NIH Establishes Stem Cell Registry, Website

Margaret Jacobs, Program Director for Epilepsy, NINDS



Much has been in the news lately, both political and scientific, about the potential role for stem cells in treating a host of diseases for which currently there are no cures.

The tremendous plasticity exhibited by stem and progenitor cells raises the possibility that they can be used to replace cells and restore vital functions that have been compromised by congenital disorders, developmental malfunction, injury or disease. In addition to cell and tissue therapy, the ability to selectively produce one or more differentiated cell types at will from pluripotent stem cells would be of clinical importance in investigating the effects of drugs and environmental factors on differentiation and cell

function in the human nervous system.

In animal studies, multipotent progenitor cells from many different sources have been reported to generate cells with neuronal or glial properties, raising expectations that they could be used to replace lost neurons and glia, repair defective circuits, and restore lost function. These studies show that of the many types of progenitor cells competent to develop neuronal and glial features, embryonic stem (ES) cells, derived from embryos at the blastocyst stage, may have the broadest natural potential and a capacity for nearly unlimited self-renewal.

On August 9, 2001 President Bush announced that federal funds can be awarded for research using human ES cell lines that meet certain criteria. To implement this new policy, and to facilitate research using these

cells, NIH created a Human Embryonic Stem Cell Registry (<http://escr.nih.gov>) listing cell lines that have been determined to meet the eligibility criteria. In addition, the NIH has great interest in supporting a wide variety of stem cell research ranging from their basic biology to pre-clinical applications in animal models of injury and disease. An understanding of factors that govern the activities of these cells is crucial in order to develop safe and effective treatments.

Many of the initiatives developed by the NIH can be found at a stem cell website developed by the NINDS (<http://www.ninds.nih.gov/stemcells>). The hope is that federally funded investigators will take full advantage of these new opportunities and explore the enormous promise of stem cells.

## PRACTICE RX

## AED Shortages Updated

Gregory L. Barkley, M.D., Chair, Practice Committee

The Epilepsy Foundation PAB leadership of the and the AES Practice Committee continue to keep close watch on the shortages in antiepileptic drugs. As you know, AED shortages seem to be an ongoing problem for families, as well as for clinical centers that rely on these products for diagnosing and treating epilepsy. Shortage reasons vary, but often involved difficulties encountered in manufacturing or unanticipated upswings in demand. The following update, prepared with the kind assistance of EF's PAB chair Patricia Osborn Shafer, RN, M.N., offers information on recent shortages and provides contact numbers for emergencies.

**AMYTAL (SODIUM AMOBARBITAL)** Ranbaxy Pharmaceuticals, manufacturer of the finished product, reports that the manufacturer of the active pharmaceutical ingredient in AMYTAL has questioned the economic value of producing a product with such small usage volume. Ranbaxy recognizes the clinical value of AMYTAL and wants to continue producing the product. The company asked AES for support concerning the medical rationale for the product; in response, Jim Grisolia sent an eloquent letter on behalf of the Advocacy Committee of the EF Board of Directors, and

I commented on behalf of the AES Practice Committee and the Board of the National Association of Epilepsy Centers. If you wish to express your opinion on the importance of AMYTAL, contact Chuck Caprariello, Vice President Business Development, Ranbaxy Pharmaceuticals Inc., 600 College Road East, Princeton, NJ 08540. *Emergency, call 888-RANBAXY or (800) 472-4467.*

**Carbatrol (CARBAMAZEPINE)** Shire Pharmaceuticals reports that the company is working to eliminate spot shortages of Carbatrol existing in some areas of the U.S. *Emergency, call (800) 536-7878, Ext. 7011.*

**IV Phenobarbital** Some shortages of injectable phenobarbital have been reported. Abbott Laboratories, manufacturer of two packaging of Luminal (PB), report that supplies of Luer 2343 (syringe without needle) are low but supplies of Sharp 2343 are adequate. *Emergency, call (800) 222-6883.*

**Keppra (LEVITIRACETAM)** UCB advises that it is increasing its manufacturing capacity to eliminate the current current spot shortages of Keppra, which UCB reports are due to an unexpected increase in demand. *Emergency, call 800-477-7877, Ext 7.*

**Tegretol and Tegretol XR (CARBAMAZEPINE)** All strengths of Tegretol and Tegretol XR are available. However, Tegretol XR supplies are not as yet at normal levels. Novartis reports that shifting Tegretol XR production to a new manufacturing facility has created temporary backorders, which the company expected to be eliminated by late February. Novartis emphasizes it is dedicated to the epilepsy market and expects the change in manufacturing facilities to eliminate long-term shortage issues. *Emergency, call (800) 526-0175.*

**ACTH Gel** ACTH gel has fluctuated in availability for the past few years. Recently Questcor purchased the manufacturing license for ACTH from Aventis who had acquired it from its Rhone-Polenc partner. Questcor can be reached at (510) 400-0700. Kenneth Greathouse is the vice president of sales and marketing.

If you encounter other shortages, please contact Patty at [pshafer@caregroup.harvard.edu](mailto:pshafer@caregroup.harvard.edu), Peter Van Haverbeke at [petervanhaverbeke@efa.org](mailto:petervanhaverbeke@efa.org), Cheryl-Ann Tubby at [ctubby@aesnet.org](mailto:ctubby@aesnet.org), or me at [barkley@neuro.hfh.edu](mailto:barkley@neuro.hfh.edu).

# Highlights of the 2001 AES/ACNS Joint Meeting

**Phi**La**del**phia  
AES&ACNS Nov. 30 - Dec. 5, 2001



Attendance topped 2,590.



Several general sessions featured panel discussions.



The Exhibit Hall opened with a ribbon-cutting ceremony and a reception.



The Exhibit Hall housed the largest group of exhibits ever.



The AES membership booth ran a preview of the revamped AES Web site.



Incoming president Tom Sutula, M.D., Ph.D. (l) received the gavel from past president Nico Moshé, M.D., shown with Executive Director Suzanne Berry.



Lennox Award presentation to Elving Anderson, Ph.D. by Nico Moshé, M.D., Robert Schwarcz, Ph.D. and Joyce Cramer.



Milken Award presentations, Nico Moshé, M.D; Daniel Lowenstein, M.D. (Basic Science), Suzanne Berry, Allen Hauser, M.D. (Clinical Science) and Jules Lesner (Milken Family Foundation).



Poster sessions were extended to a full day.

Attendees caught up on the latest in epilepsy products and services.



Opening General Session



The Philadelphia Museum of Art provided the venue for the 2001 special event.



Perry Awardee,  
John M. Freeman, M.D.



Service Awardee,  
Robert J. Gumnit, M.D.



Lennox Lecturer,  
John W. Swann, Ph.D.



Herbert H. Jasper  
Awardee, Juhn Wada,  
M.D.



Pierre Gloor Awardee,  
Gregory L. Holmes, M.D.

## 2001 Epilepsy Research Awards Presented to Drs. Hauser and Lowenstein

At the December 2001 AES/ACNS joint meeting in Philadelphia, American Epilepsy Society/Milken Family Foundation Epilepsy Research Awards were presented to W. Allen Hauser, M.D., and Daniel H. Lowenstein, M.D. The awards, given annually since 1989, are designed to recognize professional excellence reflected in a distinguished history of research or important promise for the improved understanding, diagnosis and treatment of epilepsy. Active scientists and clinicians working in all aspects of epilepsy research are eligible.

Dr. Hauser, recipient of the Clinical Investigator Award, is Associate Director and Professor of Neurology and Public Health at Columbia University's Sergievsky Center in New York City. An international force in promoting the importance of careful epidemiological studies to advance knowledge and understanding of epilepsy, he built the foundation upon which many of the current advances in the epidemiology of epilepsy are now built. His research has focused on the search for conditions that are co-morbid with epilepsy, for factors associated with mortality in people with epilepsy, and for treatment interventions to prevent or modify the course of epilepsy.

Dr. Lowenstein, recipient of the Basic Science Award, has focused his research on examining how brain injury can cause epilepsy. His work has led to a series of important discoveries that include the role of axonal sprouting, the existence of neurogenesis in the dentate gyrus, and the overall import of the recapitulation of developmental programs during the brain's attempt to recover from injury. He has been a modern pioneer in changing our concept of the consequences of status epilepticus, as well as a champion of its early and decisive treatment. Dr. Lowenstein is the Carl W. Walter Professor of Neurology and Dean for Medical Education at Harvard Medical School and Director of the Program in Brain Plasticity and Epileptogenesis at Beth Israel Deaconess Medical Center.

The awards of \$50,000 each are part of the AES/MFF Epilepsy Research Award, Grant & Fellowship Program that was established in 1989. The program also provides young investigators with funding for research training fellowships and research grants. The recognition and financial support provided through the program have been instrumental in encouraging young epilepsy investigators to enter and remain in the field.

## AES CONVERSATION WITH

## Steven J. Rugens, CMP

*AES Director of Meeting Services*

A Certified Meeting Professional and member of Meeting Professionals International, Steve is active in the local MPI chapter and served on its Board of Directors for three years.

***Philadelphia was your seventh AES Annual Meeting. How did it go?***

Attendees say ours is the preeminent meeting in the epilepsy field. They come because of the education and the new research that's presented for the first time. This year we had the largest exhibit hall ever in the history of the meeting. There were nearly 60 exhibiting companies that used over 200 exhibit booths—a very impressive hall. And the special event was sold out again. Registration for Philadelphia was 2,590; we held steady from last year despite some drop-off in international groups with the travel slowdown after September 11.

***What meeting changes did September 11 cause?***

September 11 has had an incredible impact on the meeting and tourism industry. For the first time at AES, we required people to present a photo ID at check-in in order to get their badge. I met with convention center representatives and city police in advance to talk about security. A Philadelphia Police substation was around the corner from the hotel, and there was more of a uniformed police presence at the meeting. We also increased security for the Exhibit Hall and poster sessions and had door monitors at all general sessions.

***What changes have you seen in the meeting since 1995?***

We had 1,687 attendees in Baltimore, my first year with AES. There's been increased interest in the meeting, more exhibitors, and larger numbers of abstract submissions. The poster sessions have expanded to a full day and we've added the cyber café. AES has outgrown the average hotel; we have to go into a convention center now. We've already contracted with convention centers and adjacent or nearby hotels through 2006.

***How soon in advance do you start the planning process?***

Our members like being in larger cities where there's plenty to do nearby. For cities

with major hotels and convention centers, five years out is really the minimum to get preferred dates and better rates. I do an initial site visit five years in advance, then go out with our general services contractor 18 months ahead to figure out decorating, flow, registration, signage; then once more with the AV coordinator to plan staging and room setups.

We have multi-year agreements in place with our contractors. It helps lock in pricing. And with the same people working on our meeting from year to year, they've become part of our team and have developed a thorough understanding of the AES meeting.

***What's your day like during the meeting?***

There are multitudes of details to manage and staff is often simultaneously pulled in several directions. The most important part of my job is relationships. If there's a breakdown in communication with the photographer or hotel staff or the vendors — if the message I send isn't the message they receive—that can be a problem.

The staff start work around 6:30 a.m. and we often go until late evening. The phones, the badges, the computers, the bags, the rooms, the food, audiovisual—it's all coordination and I oversee the logistics. The irony of good planning is this: a successful meeting looks like it just came together.

***What do you like best about your job?***

There are so many disparate parts and pieces to the meeting. I like seeing it all come together. I get to meet people from different walks of life and different parts of the country, and I find learning new ideas interesting and rewarding. And there's a lot of satisfaction when an AES member tells me that the work I do is important because it is helping find a cure for epilepsy.

***We're Interested!***

Please send news of appointments, honors, and awards to:

AES People in the News  
342 North Main Street  
West Hartford, CT 06117-2507

## AES CIRCUIT

**Website Features Streamlined Navigation**



Attendees of the 2001 AES/ACNS joint meeting in Philadelphia recently got a “techno-taste” of the revamped AES website, which has a new look and streamlined navigation. A self-running PowerPoint presentation was shown at the AES membership booth at The Pennsylvania Convention Center throughout the meeting last December.

Some of the latest highlights are profiled below—but to see the full range of changes and features, be sure to visit the AES site [www.aesnet.org](http://www.aesnet.org).

**LiveWire!** The new basic science discussion forum is up and running with more than 170 subscribers. Activity on the list will pick up as the number of subscribers increases, so sign up now to get in on the discussion. Go to the website and click on the button that says “Subscribe to LiveWire!”

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## Recent Advances in Epilepsy Research

(continued from page 1)

recent studies address this issue and support the hypothesis that hippocampal sclerosis may be progressive in humans.<sup>2-4</sup> Using volumetric MRI and pathological evaluations, Fuerst and colleagues did a cross sectional study of 46 patients with unilateral temporal lobe epilepsy.<sup>2</sup> They found the severity of hippocampal sclerosis and the degree of hippocampal volume loss correlated with the duration of epilepsy, especially if seizure onset was at less than 10 years of age. Patients with a history of febrile seizures had more severe hippocampal pathology. Early seizure onset and long duration of seizures was also associated with poorer performance on cognitive testing. Briellmann and colleagues reported a patient who had developed progressive hippocampal atrophy on an MRI scan, following only a few brief generalized tonic-clonic seizures.<sup>3</sup> Finally, Schulz and Ebner described a case of monozygotic twins with history of febrile seizures.<sup>4</sup> The twin who experienced complex febrile seizures lasting over 7 hours developed epilepsy and hippocampal atrophy while the twin who had only brief febrile seizures did not. Taken together, these indicate that seizures may produce some neuronal damage in certain individuals, even after a short number of seizures. This suggests that, at least in a subset of people, treatment with anti-epileptogenic agents may be beneficial.

### Identification of Molecular Mediators of Epilepsy

Multiple laboratories are working to identify the molecular changes that lead to increased neuronal excitability. Alterations in GABA<sub>A</sub> and NMDA receptor subunit composition have been found in neurons for cortical dysplasia.<sup>5</sup> The presence of antibodies to a subtype of glutamate receptor, GluR3, were found in the serum and CSF of some patients with partial epilepsy.<sup>6</sup> These findings indicate that alterations in excitatory and inhibitory neurotransmission are present in some patients with epilepsy.

Over the past year, the molecular basis for seizures in some genetic types of epilepsy have been identified. Independent studies have shown that mutations of the  $\alpha 2$  subunits of the GABA<sub>A</sub> receptor are seen in families with generalized epilepsy syndromes.<sup>7,8</sup> A family with childhood absence epilepsy and febrile seizures has been described in which a mutation in the GABA<sub>A</sub> receptor abolished natural sensitivity to

benzodiazepines.<sup>7</sup> In a separate study, Baulac and his colleagues studied a family with autosomal dominant febrile seizures with generalized epilepsy.<sup>8</sup> They identified a mutation in the  $\alpha 2$  subunit of the GABA<sub>A</sub> receptor which resulted in decreased GABA currents. These are the first reports of GABA<sub>A</sub> receptor dysfunction in familial epilepsy syndromes. Mutations in potassium channels continue to be implicated in the pathogenesis of seizures. In patients with chromosome 1p36 syndrome, when the deletion involves the region encoding a subunit of a voltage gated potassium channel, the affected individual has epilepsy. However, when the deletion did not involve the region of the chromosome encoding the potassium channel subunit, seizures were not part of the phenotype.<sup>9</sup>

### Pharmacogenomics

In an attempt to determine if medical intractability is related to altered responsiveness to antiepileptic agents, Dombrowski and colleagues applied a pharmacogenomic approach to understand medically refractory focal epilepsy.<sup>10</sup> Using cDNA arrays, the expression of multiple drug resistance genes in endothelial cells from patients with refractory epilepsy was compared to endothelial cells in vessels obtained from aneurysm surgeries. The levels of expression of several drug resistance genes were increased in the endothelium of epileptic tissue. The increased protein expression of one MDR protein was verified, indicating that increased expression of the gene resulted in an increase in the amount of protein in brain endothelial cells. These results suggest that changes in MDR expression may lead to pharmacoresistance by altering the permeability of AEDs across the blood-brain barrier. However, the variables of drug exposure and the effect of seizures were uncontrolled. The epileptic tissue had been exposed to multiple anticonvulsant medications. This was not the case with tissue from the aneurysm resections. This study suggests that inhibitors of drug resistance genes may play a role in the treatment of medically refractory epilepsy.

The effectiveness of vigabatrin for the treatment of infantile spasms was affirmed in a recent study by Elterman.<sup>11</sup> Illustrating the concept of pharmacogenomics this study identified a population of patients with a high rate of response to treatment. Vigabatrin was significantly more effective for spasms

due to tuberous sclerosis than to spasms due to any other cause. More than 50% in the tuberous sclerosis group had cessation of spasms by 2 weeks, and virtually all of the tuberous sclerosis patients responded by 3 months, compared to only 10% of patients with postnatal or dysgenetic causes of spasms. Vigabatrin was well tolerated. Insomnia, irritability and sedation were the most common adverse reaction. No visual changes were reported. However, a cautionary note about the use of vigabatrin. When studied systematically, the incidence of bilateral concentric visual field constriction was recently reported to be as high as 40%, and it was severe in 13%.<sup>12</sup> No significant recovery was observed after discontinuation of the medication, even up to 3 years after vigabatrin was stopped.<sup>12,13</sup>

### Localized Treatment

Clinical research indicates that surgical management of epilepsy is one approach to a cure, at least in patients with temporal lobe epilepsy. In the past year, several authors have reported on the effectiveness of currently available therapies for partial onset epilepsy. A controlled study compared the effectiveness of anterior temporal lobectomy to continued medical therapy in patients with complex partial seizures.<sup>14</sup> Patients who were candidates for anterior temporal lobectomy were randomized into two groups. The first group had an anterior temporal lobectomy while the second group of patients received medical therapy with antiepileptic medications. Forty patients were assigned to each group. After one year, 58% of the surgical group was seizure free; however, only 8% of the medically managed group was seizure free ( $p < 0.001$ ). The surgical group also had statistically significant reduction in seizure frequency and seizure severity, as well as an improved quality of life.

The identification of medically refractory patients can be done relatively rapidly. In a prospective study of 525 patients with recently diagnosed epilepsy, 63% became seizure free for at least one year.<sup>15</sup> Among those who continued to have seizures, only 14% became seizure free on a second anticonvulsant drug and less than 5% responded to a third. The response rate to a second agent was considerably higher if the treatment failure was due to side effects than due to lack of efficacy of the first agent. In a

Continued on page 10

**Recent Advances in Epilepsy Research***(continued from page 10)*

separate study, it was demonstrated that the majority of patients with localization related partial epilepsy (57%) become seizure free on medication. Patients with mesial temporal sclerosis were less likely to respond medically than those with other pathologies (arteriovenous malformations, tumors, infarction, atrophy, and cortical dysplasia).<sup>16</sup> Therefore Kwon and Brodie demonstrated that although many patients with lesional focal epilepsy become seizure free, patients who failed to respond to one or two antiepileptic medications will be difficult to control medically.

These clinical results indicate that epilepsy surgery should be considered relatively early in the course of treatment in patients with mesial temporal lobe epilepsy because surgical treatment is more likely to achieve a seizure free outcome, without medication side effects. However, even in this selected population, surgery is not without risks, including decline in memory function. While anterior temporal lobectomy appears to be a cure for intractable epilepsy due to hippocampal sclerosis, this etiology accounts for a minority of patients with a medically intractable epilepsy. Approximately one half of patients with focal epilepsy due to MRI visualized cortical dysplasia will become free of disabling seizures following surgical resection.<sup>17</sup> Patients with complete resection of the MRI apparent lesion are twice as likely to become seizure free (58% vs. 27%) than those with incomplete resection. Results from surgical management of non-lesional focal epilepsy have been less promising. Additionally, patients with generalized epilepsy syndromes, multifocal epilepsy, and those patients with seizures originating from functional areas of cortex are not candidates for this treatment. Therefore, the search for an alternative in curative approaches such as localized drug delivery systems continue.

For microstimulation or focal drug delivery systems to be effective methods, early detection of seizures is needed. Multiple paradigms for seizure detection are being developed. Jerger and colleagues compared seven different methods in their ability to detect intracranially recorded seizures.<sup>18</sup> All of the methods were successful in anticipating seizures one to two minutes before a seizure was identified by a neurologist. This 1-2 minute time period is probably sufficient for local treatment strategies to be effective when they are developed.

Series of surgical outcome for intractable epilepsy continue to demonstrate the importance of the complete resection of the epileptogenic zone. The outcome is poorer when lesional series are compared to non-lesional cases and when incomplete resection of the lesion is done. A recent study using diffusion tensor MR imaging in cortical dysplasia demonstrated that there are diffusion abnormalities that extend beyond what is seen on conventional MRI.<sup>19</sup> Unfortunately, it is currently unknown if the changes seen with diffusion tensor MRI identify areas of increased epileptogenicity or if diffusion tensor imaging can identify occult cortical dysplasias that are not currently seen with conventional imaging. This is the type of research that the NINDS is trying to promote with its new initiative.

**Summary**

Research towards finding a cure for epilepsy is progressing. Advances in the understanding of the molecular alterations associated with epilepsy continue. Recent data have become available which help clinicians identify patients with medically refractory focal epilepsy, and a controlled study demonstrated that surgery is a more effective treatment than currently available medications for selected patients. With future research involving multiple fields of study it is hoped that the number of patients that can be effectively treated will broaden.

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5-9

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