### **VOL. 24 • NO. 1 • FEBRUARY 2009**

# NEUROLOGY

### THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

## **PAANS: Reaching Out to Future Neurologists**

#### BY MARY ELLEN SCHNEIDER Elsevier Global Medical News

s Africa faces a growing burden of neurologic diseases and a severe shortage of both basic and clinical neuroscientists, relief is likely to come with the recruitment of a new generation of neuroscientists.

Leaders in the African neuroscience community recently took the first steps in getting young Africans interested in careers in the neurosciences. In a joint effort between the International Brain Research Organisation, the Society of Cameroonian Neurologists, and the University of Yaounde 1 in Cameroon, organizers of the Pan African Association of Neurological Sciences (PAANS) Congress 2008 devoted their pre-Congress activities to getting local students interested in the neurosciences.

The neuroscience outreach program—Neuroscience in Africa: Raising the Next Generation and Changing Attitudes to Epilepsy—was aimed at stimulating students' interest in the brain, brain disorders,



After the official opening ceremony of the PAANS 2008 Congress, Vice Prime Minister HE Amadou Ali (center, in dark suit) poses with members of Government, the new PAANS President, Dr. Alfred K. Njamnshi (immediate left), the President of the WFN, Dr. Johan Aarli, (immediate right), immediate past PAANS President (seventh from left), the President of the ILAE (far right), and other dignitaries and laureates of the Neuroscience Contest, who are wearing color T-shirts.

and neuroscience research. In addition, the organizers of the program sought to educate participants about epilepsy, including how to care for people living with epilepsy and measures that can help prevent the disorder. They also tried to make students aware of the potential career opportunities available in the neurosciences.

The need for neurologists in Africa is striking. The World

Health Organization estimates that there is an average of 0.03 neurologists per 100,000 individuals in Africa, compared with 4.84 in Europe. At the same time, the burden of neurologic disease continues to grow. Neurologic problems such as epilepsy, dementia, stroke, and headaches are common among patients seeking care in primary care settings throughout Africa and have a significant impact on productivity and quality of life.

As part of the pre-Congress activities at the PAANS Congress last October, the organizers invited primary school, high school, and undergraduate students to participate in a neuroscience competition. They also surveyed the participating students on their knowledge and

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From North America: Neurology in this region was robust in 2008, despite economic and political challenges and concerns about a possible shortage of neurologists. PAGE 10

## **European, New U.S. Guidelines for SAH Share Commonalities**

### BY JEFF EVANS Elsevier Global Medical News

**S**peedy diagnosis and treatment of aneurysmal subarachnoid hemorrhages at centers that treat relatively large numbers of patients with the life-threatening condition are crucial to reduce the likelihood of death or complications that develop following presentation and after a procedure, according to new management guidelines issued by the American Stroke Association.

The development of new endovascular techniques and diagnostic methods, as well as changes in practice patterns, has necessitated an update of the guidelines, according to an 11-member panel that wrote up the recommendations. The first edition of the guidelines was published in 1994 (Stroke 1994;25:2315-28).

The writing group performed a systematic literature review of all relevant randomized clinical trials or nonrandomized concurrent cohort studies that were published during 1994-2006 (Stroke 2009 Jan. 22 [Epub doi:10.1161/ STROKEAHA.108.191395]). Although the European Stroke Organisation has not yet published specific guidelines focused on subarachnoid hemorrhage (SAH), single European countries have been provided with recommendations by their neurologic or neurosurgical societies. Many aspects of the U.S. aneurysmal SAH guidelines are in good agreement with most of the recommendations of these societies or common European clinical practice. This is particularly true for the SAH guidelines of the German Neurological Society (version 2008), which contains similar recommendations that are based on much of the same scientific basis in regard to most facets of the disease, according to Prof. Werner

### See Guidelines • page 4

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## **EDITOR IN CHIEF'S COLUMN Changing Times**

n this issue of WORLD NEUROLOGY, we have an obituary for Raymond D. Adams, a pioneer of modern American neurology, and in the last issue we ran an obituary for Edwin R.

Bickerstaff, one of the outstanding clinical neurologists of our times. We are going through a change of the generations.

The term neurology dates back to the 17th century when it was coined by a British doctor and researcher, Thomas Willis, to describe the study of the peripheral nervous system. Subsequently, the central nervous system

was added. Initially, the field provided a framework within which diseases associated with the nervous systems could be identified. Then, in the early to middle 19th century, the principal science of neurology shifted focus to the clinical-pathological correlation. Investigators during that time included the French neurologist and pathologist Jean-Martin Charcot, and Samuel Alexander Kinnier Wilson, the American-born British neurologist. And so the torch has been passed on through the decades and into the present by giants like Dr. Adams.

When I did my training, the great neurologists were those who could examine a patient with an exquisite technique-not unlike the skill, clarity of execution, and technical excellence we see in a violin virtuoso-and then come up with the right answer. C. Miller Fisher likes to tell the story



HALLETT, M.D.

that when he and Dr. Adams worked for Derek Denny-Brown at the Boston City Hospital, the New Zealand-born neurologist initiated a weekly "brain cutting" session. They all would make

predictions about the pathology on the basis of their clinical findings, and they would be "wrong, wrong again." There was still work to do, and Adams Bickerstaff Fisher and others continued to make important clinicalpathological correlations. Much of that work has

been done now, and we can be right much of the time. Not all the time, of

course. Neurology is a diverse field with extraordinary variety. Clinicalpathological correlation for the practitioner is aided by spectacular advances in neuroimaging-though I still can't help feeling this is cheating.

These days, the major advances in neurologic disease are being made at the molecular level. Advances in cell biology and genetics are providing fascinating insights. A few years ago, we did not even think that Parkinson's disease had a genetic factor, and now it is becoming clear that most, if not all cases, do. Medications (and surgery) have been developed based on our newfound understanding at the molecular and basic physiological levels. We still have not converted our genetic understanding into many therapies, and stem cells are pie in the sky, but that is the probable future.

It is emerging that even some clinical-

pathological correlation is confusing. For example, a patient with a frontotemporal dementia and another with parkinsonism with a dystonic, apraxic arm might have similar pathology of corticobasal degeneration. If we consider molecular pathology, it can become even more confusing: A type of ataxia (SCA6) and hemiplegic migraine are a result of a mutation on the same gene, and stiff person syndrome, ataxia, or epilepsy might be due to anti-GAD antibodies (described by Francesc Graus and Albert Saiz in the December issue of World Neurology).

The era of clinical-pathological correlation is drawing to a close, and the days of molecular biology are ahead. The neurologists who are making important advances are often at the bench and not at the bedside. We are hopeful that translations to useful therapies will follow.

However, while the generations are changing, some things stay the same. There are important lessons from neurologists like Raymond Adams. And here, I will speak from personal knowledge, because he was my advisor in medical school as well as my residency chief. His lesson was the same as that of another of my mentors, the Japanese neurophysiologist Ichiji Tasaki, who passed away in January: Don't necessarily believe what you read, make your own careful observations, think logically about them, and come to your own conclusions. You may be right more often that way, and you might be able to make a new observation that will move Neurology forward.

## **WFN Elections** 2009: Nominating **Committee Recommendations**

he Nominating Committee of the World Federation of Neurology invited nominations for three officer posts and one trustee to be elected at the Council of Delegates Annual General Meeting in October at the World Congress of Neurology in Bangkok.

The committee now recommends to the membership those listed below as candidates in accordance with the Federation's Memorandum and Articles of Association.

President (from Jan. 1, 2010)

Jagjit Chopra (India) Vladimir Hachinski (Canada) First Vice President (Jan. 1, 2010)

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Secretary-Treasurer General (Jan. 1, 2010) Wolfgang Grisold (Austria) Raad Shakir (U.K.)

One Elected Trustee (Oct. 2009) Wolfgang Grisold (Austria) Orla Hardiman (Ireland)

Candidates for President and First Vice President will be required to formulate a statement of their goals and objectives for the organization, which will be published.

Anyone can make additional nominations by securing the supporting signatures of five or more authorized WFN Delegates, or by submitting the name(s) of the individual(s) to the Secretary-Treasurer General, c/o the WFN Headquarters Office, Hill House, Heron Square, Richmond-Upon-Thames, TW9 1EP, U.K., at least 30 days before the date of the Council of Delegates' Annual General Meeting.

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WORLD NEUROLOGY, an official publication of the World Federation of Neurology, provides reports from the leadership of the WFN, its member societies, neurologists around the globe, and news from the cutting edge of clinical neurology. Content for WORLD NEUROLOGY is provided by the World Federation of Neurology and Elsevier Global Medical News

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Address Change: Fax change of address to +1-973-290-8245

**POSTMASTER:** Send change of address (with old mailing label) to World Neurology, Circulation, 60 B, Columbia Rd., 2<sup>nd</sup> Fl., Morristown NJ USA 07960

World Neurology, ISSN: 0899-9465, is published quarterly by Elsevier Inc., 60 B, Columbia Rd., 2nd Fl., Morristown NJ 07960. Phone +1-973-290-8200; fax +1-973-290-8250.

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he World Congress of Neurology is an important rendezvous for our profession. There are many opportunities for neurologists to meet, such as our regional conferences; the annual

conferences of the American Academy of Neurology; and the international congresses of epileptology, Parkinson's disease and related disorders, headache, multiple sclerosis, and other sectors in the field.

Nevertheless, the WCN's quadrennial meetings-which this year will become biennial-remain the most effective venue for the presentation of scientific achievements and for interaction among dele-

the number of contributions.

gates from varied backgrounds and with

diverse perspectives. The gatherings are

also crucial for the visibility of the orga-

nization; the number of participants has

increased steadily over the years, as have

opportunity for young neurologists to re-

ceive updates on developments in the

neurosciences. Some of them will be

World congresses also offer a unique



AARLI, M.D.

able to present their own research data, and even more will get to make new friends and meet up with old ones.

Such interaction is an important component of any international congress, so

> this year the World Federation of Neurology is offering twice the number of travelling fellowships for young neurologists from countries classified as low- or lowermiddle income by the World Bank to attend the congress.

THE PRESIDENT'S COLUMN

**Destination Bangkok** 

This year, the World Congress of Neurology will take place in Thailand, at the Bangkok International Trade & Exhibition Centre, Oct. 24-30. Professor Niphon Poung-

varin, the congress president, will welcome us to this beautiful, exotic city. Dr. Naraporn Prayoonwiwat, local chair of the Scientific Program, and Prof. Roger Rosenberg, chair of the WFN Research Committee, have put together an outstanding scientific program. The main themes, assembled under the common heading of "Innovation in Neurology," will be stroke, epilepsy, neurogenetics,

multiple sclerosis, dementia, movement disorders, headache, and pain.

In addition, there will be a broad education program offering 27 half-day and full-day teaching courses in a variety of topics, which has been organized by Prof. Siwaporn Chankrachang, chair of the local Education Programs, and assisted by the WFN Education Committee chaired by Prof. Theodore Munsat.

At the XVII World Congress of Neurology in London in 2001, we launched our first Neurological Tournament, a knockout competition in which teams of delegates from countries represented in the WFN participate. Similar tournaments have for many years provided educational entertainment at the meetings of the American Academy of Neurology. The London tournament was a great success and was repeated at the XVIII World Congress of Neurology in Sydney in 2005. This year, Disya Ratanakorn and the coordinators of the tournaments at the London and Sydney congresses, will organize the 3rd Tournament of the Minds at the Bangkok congress. We look forward to an exciting competition that no doubt will bring with it a special Thai flair.

Organizing a congress of this scope and nature is an immense task, and the chair of the local Organization Committee, Dr. Pairoj Boonkongchuen, together with the Congress Chairman Kammant Phanthumchinda, Somsak Laptikultham (Secretary), Somchai Towanabut (Treasurer), and conference coordinator Kate Sarasin have worked for endless hours to ensure the smooth running of this year's congress. Their aim is to make it a worthwhile and attractive experience during which the delegates can enjoy the rich and exciting scientific program in an exotic and intriguing setting. We all look forward to gathering in Bangkok in October.

### World Congress of Neurology

Bangkok, Thailand (Oct. 24-30, 2009) Plans for the Congress are progressing well. We encourage neurologists from across the world to submit abstracts and utilize the early registration window. For details, go to www. wcn2009bangkok.com.

Johan A. Aarli, President, WFN Niphon Poungvarin, President, WCN

### WFN Research Group **Defines Standards** In Neurosonology

BY MANFRED KAPS, M.D.

For more than 30 years, the Neurosonology Re-search Group has provided an international podium for the presentation of scientific advances and the promotion of research, education, and training in ultrasonic techniques.

The group consists of a worldwide pool of more than 300 technological and clinical experts in neurosonology. Statutory meetings take place every 2 years, with numerous local meetings and regional teaching courses in between.

Our main meetings with general assembly rotate from continent to continent. The last meeting was in 2007 in Budapest, Hungary, and the next will be held Sept. 4-6, 2009, in the Asian-Pacific region at Cairns, Australia. It will take place in association with the 6th Asian Pacific Conference Against Stroke, organized by Australian and Asian neurologists-Craig Anderson, Christopher Levi, Jose Navarro, N.V. Ramani, L. Wong, and Shan-Jin Ryu. The main topics will be ultrasound in clinical research; standards in neurosonology; sonothrombolysis, including technical updates; functional testing; and monitoring during interventions.

The NSRG will provide platform presentations from basic research to clinical application and the process of certification will be carried forward. It also will be active at the World Congress of Neurology in Bangkok in October, where we will make contributions in the main program and offer a full-day teaching course on Oct. 25, before the congress. In particular, we invite young researchers to join us. Cerebrovascular ultrasound is a rapidly developing field with many innovative aspects, and the NSRG offers a stimulating forum for new ideas and for establishing global contacts. For more information, visit www.nsrg.org.tw.

## **HIGHLIGHTS: THE JOURNAL OF NEUROLOGICAL SCIENCES Cryptogenic New-Onset Refractory Status Epilepticus in Adults**

Four patients had a mild febrile ill-

ness in the 2 weeks before NORSE.

The sudden onset of intractable seizures is not uncommon, and all neurologists have had to manage such patients. Often, the condition can be traced back to a known cause, such as epilepsy, stroke, infection, neoplasm, or intoxication.

The most difficult cases are those where the cause is unknown, because there are few data to help guide management of these patients, apart from the direct, but by definition unsuccessful, suppression of the seizures. Thus, clear-cut therapeutic options such as antibiotics, corticosteroids, antivirals, or surgery are

not available. Since status epilepticus is not uncommon in viral encephalitis and viral encephalitis can be difficult to reliably exclude, it remains a leading candidate for the etiology of new-onset refractory status epilepticus (NORSE).

In this paper, the authors summarize the presentations, clinical course, and investigations of six patients with NORSE. The patients were previously healthy; had the sudden and unexpected onset of prolonged seizures resistant to aggressive antiepileptic therapy, even after suppression under anesthesia; and no etiology discovered despite a very extensive work-up.



**BY ALEX** TSELIS, M.D., PH.D.

> Outcomes were generally dismal in these patients (aged 24-36 years), with one death, two dependent on others for daily activities, two independent but impaired, and only one with a good outcome (J. Neurol. Sci. 2009;277:26-31).

> Dr. Daniel Costello, first author of this paper, is a staff neurologist at the Massachussetts General Hospital, in Boston, U.S.A., who became intrigued with NORSE when he saw a number of such patients while doing his epileptology fellowship. "Most neurologists, especially epileptologists, have seen these cases, but they are not common, except in large centers. The

paper [describes] six cases who were very well worked up with fairly complete data sets," he said. The cause was unclear in these cases, and "most of them were deemed to have an underlying viral encephalitis, but despite everyone's best efforts, a viral agent was never found."

The idea of a viral infection is not unreasonable, given the prodrome in these patients and the known association of seizures with viral disease. This is obvious in the case of herpes simplex encephalitis, where the risk of status epilepticus is high, but some viral encephalitides, with prominent seizures, were first clinically described decades before a specific virus was implicated. An example would be subacute sclerosing panencephalitis, caused by measles virus. A less wellknown example would be epilepsia partialis continua (Kozhevnikov's epilepsy), a known sequela of Russian spring-summer encephalitis, transmitted by ticks in eastern Siberia.

As our knowledge of viral disease expands, it is not unreasonable to expect that a viral etiology of NORSE, as well as other idiopathic diseases of the central nervous system, will be established.

DR. TSELIS is an associate professor of neurology at Wayne State University, Detroit. He is the book review editor for the Journal of the Neurological Sciences.

microglial activation and gliosis, but no specific findings. There was no clearcut beneficial response to a variety of treatments, including antivirals, antibiotics, intravenous imunoglobulin, corticosteroids, or plasmapheresis, in addition to antiseizure drugs.

## **Early Referral for SAH Essential**

**Guidelines** • from page 1

Hacke, chairman of the department of neurology at the University of Heidelberg (Germany), and Dr. Julian Bösel, a neurologist in the Neuro ICU at the University Hospital Heidelberg.

The U.S. guidelines strongly recommended surgical clipping or endovascular coiling of ruptured aneurysms with SAH to reduce the rate of rebleeding. Long-term follow-up angiography is required for ruptured aneurysms that are incompletely clipped or coiled, or for those that are wrapped or coated instead, because they have an increased risk of rehemorrhage, compared with com-

pletely occluded aneurysms. Management of patients

at centers that offer both clipping and coiling may be recommended because experienced teams of cerebrovascular surgeons and endovascular specialists at such centers can use a combination of both techniques when appropriate and tailor the treatment to individual characteristics of the patient and aneurysm. Early treatment of ruptured aneurysms "is reasonable and is probably indicated in the majority of cases" because it reduces the risk of rebleeding after SAH, ac-

cording to the writing group. The group suggested that early referral to high-volume centers that have both experienced neurovascular surgeons and endovascular specialists is reasonable, even though "it is uncertain whether the benefits of receiving care at a high-volume center would outweigh the costs and risks of transfer." The fact that overall ruptured aneurysm volume does not predict a good outcome as well as endovascular treatment of post-SAH vasospasm "may reflect the overwhelming importance of bleed severity on overall outcome."

"Procedural volume may seem more important for surgical clipping than for endovascular therapy for a variety of reasons, but perhaps the most important reason for this apparent discrepancy revolves around the fact that published results of endovascular treatment come primarily from high-volume centers, whereas results of surgical clipping come from both high- and low-volume centers," the committee added.

The writing group did not support screening for asymptomatic intracranial aneurysms in the general population or in patients with environmental risk factors, such as smoking and alcohol use, because no population-based clinical studies of its cost-effectiveness have been conducted. Screening of patients with familial intracranial aneurysm syndrome should be conducted on an individual basis, tailoring the appropriate screening modality to the patient.

Evidence from observational cohort studies suggests that antihypertensive medications and smoking cessation may

help to prevent or reduce the risk of SAH in patients with asymptomatic intracranial aneurysms. The writing group noted, however, that "no randomized controlled trials have specifically examined whether treatment of medical risk factors reduced the occurrence of subarachnoid hemorrhage.

A separate writing committee has been commissioned to update recommendations for the management of unruptured intracranial aneurysms, which were last published in 2000.

Because the severity of the initial bleed is the most useful indicator of outcome following an aneurysmal SAH, the committee recommended using grading scales that rely heavily on it to plan future care with family and other physicians. Rapid diagnosis and treatment is the most important goal for patients with suspected SAH because rebleeding, which is most likely to occur within the first several days after the initial bleed, "is currently the most treatable cause of poor outcomes," the panelists wrote.

Outside of the classic SAH presentation of the quick onset of a severe headache and signs and symptoms such as nausea with or without vomiting, stiff neck, brief loss of consciousness, or focal neurological deficits, some patients experience symptoms that are consistent with a "sentinel bleed" or "warning

The importance of recognition of a warning leak cannot be overemphasized. Headache is a common presenting chief complaint in the [emergency department], and SAH accounts for only 1% of all headaches evaluated in the ED. Therefore, a high index of suspicion is warranted," the writing group advised.

The guidelines continue to recommend diagnosing SAH with noncontrast cranial CT scanning, supplemented by a diagnostic lumbar puncture if the initial scan is negative. The group strongly recommended the use of selective catheter cerebral angiography to locate the presence and anatomic features of aneurysms in patients with documented SAH. MR or CT angiography may be useful in patients with a negative cranial CT scan and equivocal lumbar puncture results or when conventional catheter angiography "cannot be performed in a timely fashion."

To prevent rebleeding of an SAH, the guidelines advise bed rest and controlling hypertension with short-acting continuous-infusion intravenous agents with a reliable dose-response relationship and favorable safety profile, such as nicardipine, labetalol, and esmolol. Some evidence suggests that a short course of antifibrinolytic agents, in combination with early aneurysm treatment, may be reasonable if it is followed with

prophylaxis against hypovolemia and vasospasm. This may help to reduce ischemic complications that result from antifibrinolytic therapy while still reducing preoperative bleeding rates.

To manage cerebral vasospasms, the committee highly recommended the use of oral nimodipine to reduce poor outcomes. The value of other calcium antagonists remains uncertain. In most cases, maintaining normal circulating blood volume and avoiding hypovolemia is "probably indi-

cated." When vasospasm symptoms arise, the writing group suggested that it may be reasonable to expand volume (hypervolemia), induce hypertension, and start hemodilution-known as triple-H therapy—or alternatively, to perform cerebral angioplasty with or without selective intra-arterial vasodilator therapy.

When chronic, symptomatic hydrocephalus arises after SAH, the committee recommended temporarily or permanently diverting cerebrospinal fluid. A ventriculostomy may be beneficial in those who develop ventriculomegaly and decreased level of consciousness.

The committee did not recommend long-term use of anticonvulsants to prevent seizures associated with SAH on a

sued a report on the outreach project. Immediately following the program, many of the student participants said they would consider a career in the neurosciences.

The organizers of the outreach program are still analyzing the results of the knowledge and attitudes survey to better understand the impact of the brief educational activity offered to students. However, the full impact of the outreach program cannot be fully assessed in the short term, they wrote in their report.

routine basis, but thought that their use may be considered in the immediate posthemorrhagic period.

When hyponatremia occurs after SAH, the panelists generally recommended avoiding administering large volumes of hypotonic fluids and preventing intravascular volume contraction.

Four members of the U.S. writing group reported having potential conflicts of interest with relevant companies, including research support, speaking or consulting, and having ownership interest.

In some aspects of the treatment of aneurysmal SAH, the strength of recommendations differs between the German and U.S. guidelines. The German guidelines recommend coiling in cases where the aneurysm is technically and anatomically suited for endovascular therapy, whereas the U.S. recommendations advise that "endovascular coiling can be beneficial [in aneurysms] amenable to both endovascular coiling and neurosurgical clipping," Prof. Hacke and Dr. Bösel told WORLD NEUROLOGY.

In addition, while triple-H therapy is described as "a reasonable approach" to

symptomatic cerebral vasospasms in the U.S. guidelines, it is clearly recommended in the situation of delayed ischemic neurologic deficits in the German recommendations. On the other hand, treatment options that are less well supported by scientific evidence, such as endovascular treatment of vasospasms or the use of magnesium or statins, do not reach recommendation status yet in the German guidelines, while some of them do in the U.S. recommendations. The German Neurological

The strength of

recommendations

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differ between the

U.S. and Germany.

DR. BÖSEL

Society also emphasizes the treatment of SAH patients in specialized intensive care units (i.e., neuro ICUs) and the importance of intensified hemodynamic monitoring, especially during triple-H therapy, somewhat more than do the U.S. recommendations.

Regional differences in SAH management or guidelines outside the United States and Germany seem to depend on whether neurologic or neurosurgical societies have created the guidelines, on diagnostic options, on the regionally different availability of high-volume treatment centers, on the standard of endovascular alternatives to surgery, and on the appreciation of evidence, Prof. Hacke and Dr. Bösel said.

The leaders who organized the events plan to work with the Society of Cameroonian Neurologists, PAANS, and the University of Yaounde 1 to follow the progress of the students who participated in the program over the next several years.

"The type of outreach program presented in Cameroon is important because it makes neurosciences not a foreign and exotic subject, but a part of their daily life and of public health," said Dr. Johan A. Aarli, president of the World Federation of Neurology.



Many of the U.S. guidelines are in good agreement with European societies' recommendations. **PROF. HACKE** 

leak" 2-8 weeks before an overt SAH.

### **Success Seen in African Outreach PAANS** • from page 1

attitudes about epilepsy both before and after a brief educational activity designed to raise awareness of the condition.

Three prizes were awarded in each of the three categories-primary students, secondary students, and university students. The winners received their awards at the opening of the Congress of the Pan African Association of Neurological Sciences, the largest single

gathering of neuroclinicians in Africa. The prizes were presented by the Vice-Prime Minister, Minister of Justice, Keeper of the Seal, and other members of the Cameroon Government, and other dignitaries.

The outreach activities appear to be a success, according to Dr. Rufus Akinyemi, Dr. Faustin Njionda Yepnjio, and Prof. Alfred K. Njamnshi, who is-

## Help Haitian Health by Adopting a Soccer Team

BY ANTHONY G. ALESSI, M.D.

lobal medicine is an increasingly popular area of specialization for young

physicians who are motivated by adventure and spirit of making a lasting contribution. Although most are drawn to it from primary care, neurologists are uniquely qualified to participate in these worldwide initiatives. They are taught to rely on



ANTHONY G. ALESSI, M.D.

observation as well as the neurologic history and examination, skills that are essential when caring for patients in regions where technology is not always readily available for a diagnosis.

We have seen media footage of the poverty and hunger that has gripped Haiti for decades. Located just 90 miles off of the coast of Florida, Haiti is the poorest nation in the Western Hemisphere, and although it is



relatively small, it has a popula-

It was during a recent medical

mission to the hurricane-rav-

aged island, that I came across

an inspiring story. The Haitian

Health Foundation

rounding villages.

Four times a year,

tion of about 8 million.

its founder, orthodontist Dr. Jeremiah J. Lowney, leads a week-long excursion to the island, during which physicians, dentists, and volunteers from all walks of life work with the local people. These pilgrimages are designed to benefit the poor, but it is often the volunteers who find themselves invigorated. "Over 90% of volunteers return to spend additional weeks among the poor," he said. While evaluating a girl in one

of the HHF clinics, I learned her soccer coach had accompanied her, and I was surprised to hear that women's soccer was well organized and thriving in that area.

Ordinarily, women in Haiti do not play soccer. Haitian girls, especially in remote areas, grow up believing that playing games such as soccer will deform their reproductive organs and prevent them from bearing children.

However, many girls are interested in playing the game so, in 2006, HHF started a health education and soccer program for girls aged 13-19 years. It seeks to empower girls through knowledge and education and is structured so that they have to complete a 1-week course on responsible sexuality before qualifying for the soccer league.

The classes cover topics such as reproductive anatomy, sexually transmitted diseases, and women's rights under Haitian law, with the underlying message that education is the key to better opportunity.

In the past year, almost 1,300 girls have been educated through the program and 830



Teenage girls who want to qualify for the soccer league are required to complete a 1-week course on responsible sexuality.

played in the league. "Participation in the program has become a source of pride for the girls and their parents," says Callie Kaplan, from Chicago, the program coordinator.

Unfortunately, the HHF soccer program is losing its major grant support, which could result in ending this worthwhile program. It costs \$1,000 to fund a team, which would cover the most basic equipment and the educational component. Any donation would be gratefully accepted, but I encourage any individual or business to join me in adopting a team. Donations can be sent to Haitian Health Foundation, 97 Sherman Street, Norwich, CT, 06360 or made on its Web site at www.haitianhealthfoundation.org.

DR. ALESSI is in private practice and is chief of neurology at the William W. Backus Hospital in Norwich, Conn.



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## THE PRESIDENT'S ANNUAL REPORT 2008 Outreach and Exchange

### BY JOHAN A. AARLI, M.D. President, WFN

ast year was a good one for international neurology, and we witnessed many important decisions for the future of the World Federation of Neurology.

While the World Congresses of Neurology until 2009 had been quadrennial, officials at the Annual Delegate Meeting in Brussels 2007 decided that that meeting will become biennial from 2009.

We also decided that the 2011 congress will take place on the African continent. At the Annual Delegate Meeting in New Delhi in October 2008 during the meeting of the Asian and Oceanian Association of Neurology, Marrakesh was selected as the venue for the World Congress in 2011.

In addition, Marrakesh was the venue for the successful 10th Congress of the Pan African Association of Neurological

### AN IMPORTANT TOPIC OF DISCUSSION AT THE AFRICA COMMITTEE MEETING IN STELLENBOSCH WAS THE TRAINING OF NEUROLOGISTS FROM THE AFRICAN CONTINENT.

Sciences in 1992. The increased frequency of the world congresses makes a revision of the congress contract necessary, and this work has already started.

The World Congress of Neurology 2009 will take place in Bangkok, Thailand. The Organizing Committee has been hard working and very effective, and I am pleased to report that the Scientific, Educational, and Social programs were finished long ago.

The political situation in Bangkok was occasionally turbulent toward the end of the year. However, Thailand has an international reputation as a land of smiles and a place where political problems can be solved without dramatic events. We all look forward to Bangkok as an exotic and rewarding destination in October 2009.

Biennial congresses will present a new

challenge to WFN. We have, therefore, interviewed representatives among various professional congress organizers and have appointed Kenes as a core professional congress organizer (PCO) for the world congresses of 2011, 2013, and 2015. Kenes already is the PCO for the European Federation of Neurological Societies (EFNS). The WCN 2013 will take place in Europe, and there will be no EFNS congress that year.

According to our constitution, the WFN shall hold an Annual Council of Delegates meeting every year in which all Member Societies, associate members, the Officers and the Trustees are entitled to attend. These meetings have usually taken place in the USA or Europe, but this time we decided to have it in Asia, at the 12th Asian Oceanian Congress of Neurology in New Delhi. The meeting, which was organized with the 16th Annual Conference of the Indian Academy of Neurology at the Ashok Hotel with Professor Man Mohan Mehndiratta as organizing secretary, and former president of India, A.P.J. Abdul Kalam as chief guest, became an exciting venue for presentations of excellent contributions to international neuroscience.

The Atlas of Neurological Resources, a joint publication with the World Health Organization, has underlined the seriousness of the situation for neurology in Africa. This is the background for the Africa initiative, which started in 2006, and which has gained a strong foothold in international neurology. Much happened in 2008. The Africa initiative has two arms, TAFNA (Task and Advisory Force for Neurology in Africa) and the Africa Committee. It is the Africa Committee that is drawing the road map for neurology in Africa, while TAFNA represents the advisory element.

TAFNA, which I chair with Prof. Amadou Gallo Diop, was established in London in 2006. TAFNA has a link with IBRO and SONA (Society of Neuroscientists of Africa). The Africa Committee was established at a meeting in Stellenbosch, South Africa, in 2008, with a membership predominantly of African people who are working in African countries. Prof. Diop is the chairman.

An important topic for discussion at



Attendees of the PAANS Congress in Yaoundé, Cameroon, November 2008, included, from left, Professor Adeloye (Nigeria), Johan Aarli (WFN), and Alfred Njamnshi (Cameroon). The five persons on the right are all local politicians.

Stellenbosch was the training of neurologists from the African continent. Senegal, Cameroon, and Cote d'Ivoire have well established neurological service and a good contact with France. Tunisia, Morocco, and Algeria are prime places for neurology training.

South Africa has excellent neurology departments, while the neighboring countries are smaller and have a less developed medical infrastructure. South Africa may have a capacity for training of neurologists from these countries.

The first neurologist in Namibia recently finished his training in Johannesburg. The East African countries (Kenya, Uganda, Zambia, Ethiopia, Tanzania, and Malawi) are in different situations and have at present no consensus on future training centers.

The Italian Society of Neurology recently initiated a training program for Ethiopian neurologists that may serve as a model for other national neurological societies.

The Pan African Association of Neurological Sciences (PAANS) was founded in 1972 and consists of neurologists and neurosurgeons from the African continent. I had the pleasure to attend the PAANS congress in Yaoundé, Cameroon, in November 2008. Difficulties in traveling in Africa and high air fares make attendance of PAANS difficult, but the congress was well attended despite these challenges, especially from Central and West Africa. The PAANS congress served as an important information and discussion forum for African neurology. The meeting also was attended by local politicians and representatives from the government, which is essential in increasing the visibility of neurology. Prof. Alfred Njamnshi, Cameroon, was elected president of the PAANS and is also ex officio WFN Regional Director for Africa.

The first international teaching course in neurology in Africa, which took place in Dakar, Senegal, June 26-28, was organized by EFNS and became a great success. It reflected the basic idea of the Africa initiative, With Africa–For Africa, and came as a joint venture between several international organizations, WFN, IBRO, WNFo, and PAUNS, in addition to EFNS, which was the prime organizer. EFNS already is planning the successor to this meeting, in Addis Ababa, Ethiopia, in June 2009.

In 2008, WORLD NEUROLOGY began to change its image. Dr. Mark Hallett has taken over as the new editor in chief, and the newsletter aims to emphasize new and emerging clinical and basic neuroscientific reports in the neurological literature. For 2008, we had as before four issues. This year, we might print more. We also have a new Web site, and Wolfgang Grisold is the Web site editor. I hope these changes prove positive and help increase the visibility of neurology in all parts of the world.

## **Research Committee Annual Report 2008**

BY ROGER N. ROSENBERG, M.D. Research Committee Chair, Trustee, WFN

The Research Committee has been active in supporting the Scientific Program Committee, which is chaired by Dr. Naraporn Prayoonwiwat for the World Congress of Neurology 2009 in Bangkok in October.

Dr. Roger Rosenberg, who is the Research Committee Chair, assisted in the selection of topics and speakers for the Scientific Program when the Trustees of the World Federation of Neurology met with the Scientific Program Committee in Bangkok in January 2008 and again in Delhi, India, October of last year.

The XVIV World Congress of Neurology "Innovation in Neurology" will have as its centerpiece an exciting and comprehensive Scientific Program representing all of the important fields of clinical neurology and emerging new areas of translational neuroscientific re-

search defining neurologic diseases and therapeutic advances.

Internationally recognized speakers who are scholars and authorities in clinical neurology and basic neuroscience have agreed to participate in the program. We believe it will be a program of great interest and benefit to neurologists everywhere in the world.

The Research Committee and its 30member Research Groups met in Chicago, in April 2008 in association with the annual meeting of the American Academy of Neurology. Each Research Group provided input for the WCN 2009 Scientific Program and offered ideas for the next WCN, in Morocco in 2011.

We encourage participation in the activities of the Research Committee. Those interested in getting involved should contact the Chair of the Research Group in their field of clinical neurology or basic neuroscience and share their ideas. Contact information can be obtained from the WFN by e-mailing Info@ wfneurology.org.

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## **MS in Asia: PACTRIMS Inaugural Meeting**

BY BHIM SINGHAL Past Asian-Oceanian Regional Director, WFN

The newly formed Pan-Asian Committee for Treatment and Research in Multiple Sclerosis held its first meeting at Kuala Lumpur, Malaysia, on Nov. 21-22 last year under the leadership of Dr. Takahiko Saida of Japan (President) and Dr. William Carroll of Australia (Vice President).

The organizing chairman of this very successful meeting was Professor Chong Tin Tan of Malaysia. The Scientific Committee, headed by Professor Jun-ichi Kira of Japan (Chairman) and Dr. Victor Chong of Malaysia (Vice Chairman), drew together an impressive program dealing with the epidemiology, pathogenesis, manifestations, and treatment of multiple sclerosis (MS).

More than 350 delegates from 21 countries participated in the meeting. In addition to the talks by invited speakers from the East and the West, there were 54 posters presented by investigators and dealing with a range of aspects of MS and other demyelinating disorders.

There is a growing interest in multiple sclerosis and related demyelinating disorders in the Asian region. Although the disease is less common in Asia than it is in the West, more cases are being diagnosed in the region. Improved detection methods might play a role, but there also seems to be a true increase in the prevalence of MS, which is reflected in epidemiological data from Japan and Iran. As in the West, MS in Asia has a higher prevalence in women and the average age of onset is 27-30 years. The incidence of familial cases is low; and oligoclonal bands are less commonly detected. The clinical presentation is either the classic or conventional form of MS (CMS), with involvement of brain and cerebellum as well as optic pathways and spinal cord; or the opticospinal (OS-MS) form, with manifestations restricted to optic pathways and spinal cord.

In contrast to earlier data, CMS cases seem to be on the rise, compared with OS-MS. The latter cases include patients with longitudinally extensive spinal cord lesions (LESCLs). Neuromyelitis optica (NMO) was first described as a severe monophasic syndrome of acute bilateral optic neuritis and transverse myelitis. It has now been recognized also to have a relapsing course with optic nerve involvement and LESCLs. In Asia, as in the West, it remains controversial as to whether CMS, OS-MS, and especially NMO are different disorders or different manifestations of MS.

The detection of aquaporin-4 (AQP4) antibodies has given a new tool and dimension to the study of demyelinating diseases. AQP4 has been reported to have high sensitivity and specificity in patients with an NMO-type of presentation.

AQP4 antibodies have also been found in patients with other manifestations such as recurrent optic neuritis, myelitis with longitudinally extensive spinal cord lesions, patients with intractable vomiting and hiccups, and patients with



Members of the PACTRIMS' international faculty and the steering committee gathered for the organization's inaugural meeting in Kuala Lumpur, Malaysia.

unique lesions on MRI in hypothalamus and periaqueductal regions. The antibody is directed against the water channel aquaporin-4 and believed, by some, to be the causative agent of NMO. The levels of AQP4 in the serum have been reported as being high before the onset or relapse of demyelinating disease and decreasing during remissions.

Some investigators have hypothesized that NMO has a different pathogenic basis and responds better to immunosuppressive agents than to immunomodulating agents. Some studies in the Asian region, however, have raised doubts about this hypothesis and the significance of AQP4 antibody as well as its place in the definition of OS-MS.

The arguments put forward to question this hypothesis include the point that NMO has not been associated with characteristic cerebellar lesions even though the aquaporin-4 target antigen has a high concentration in the cerebellum. Furthermore, the antibody has been found to be of low sensitivity and specificity in NMO in some Asian studies, including in white Australians. AQP4 also has been found occasionally in CMS patients.

Many specialists in the field hope that the ongoing Registry of Asia Pacific Idiopathic Demyelination (RAPID) study in the Asian region and the global MS base registry will provide useful epidemiological data and help resolve some of these issues.

The second meeting of the PACTRIMS is scheduled to be held in Hong Kong in November 2009.

For more information about the inaugural PACTRIMS meeting and the upcoming meeting later this year, visit www.PACTRIMS.org.

## **Exercise Doesn't Promote Foot Ulcers in Neuropathy**

BY HEIDI SPLETE Elsevier Global Medical News

**E**rates in adults with diabetic peripheral neuropathy, based on a study of 79 adults aged 50 years and older.

The American Diabetes Association recommends moderate physical activity for people with diabetes but also recommends that people with diabetes and neuropathy limit weight-bearing activity to reduce the risk of foot ulcers.

"This was based on a longstanding assumption that repetitive mechanical stimulation, which the feet endure during walking, would lead to foot ulcers in those with neuropathy, an assumption that has remained untested since rat foot pad studies in the 1970s," said Dr. Joseph LeMaster of the University of Missouri–Columbia.

Previous studies have shown that people with diabetes who walk regularly can reduce their risk of developing complications such as cardiovascular disease.

To determine whether regular walking increased the risk of foot ulcers, Dr. LeMaster and his colleagues conducted a randomized, controlled trial known as Feet First, in which 41 adults received an intervention that included leg-strengthening and balance exercises, directions for a self-guided walking program, and telephone support every 2 weeks. Dr. LeMaster presented the results at the annual meeting of the North American Primary Care Research Group.

Both the intervention group and a control group of 38 adults received foot care education, regular foot checks, and eight sessions with a physical therapist, but the control group received no additional exercise intervention. The average age was 66 years, and 51% were women.

After 6 months, the average number of total daily steps taken was not significantly different between the two groups, although the total steps decreased by 13% in the control group. But participants in the intervention group increased the steps taken during a 30-minute exercise session by 14% from baseline, compared with a 6% decrease in the control group.

Although the activity level was less than the researchers hoped for, the results suggest that the intervention helped avoid a decrease in activity, Dr. LeMaster said.

Overall, 22 lesions occurred in the intervention group and 14 in the control group after 6 months, but this difference was not significant. This number increased to 27 lesions in the intervention group and 21 in the control group after 12 months. The total of 48 lesions excluded 9 lesions that resulted from trauma during self-care (such as cutting a toe while trimming a toenail).

The overall ulcer rates were similar between the groups at 6 months, but by 12 months the rate of weight-bearing full thickness plantar lesions was higher in the control group, compared with the intervention group (five lesions vs. one lesion).

"We conclude that intervention achieved a modest increase in daily ambulatory activity," Dr. LeMaster said. "Prescribing these patients a carefully monitored program in which they gradually increase walking over several months is probably safe," he said. But he noted that careful attention to footwear and regular foot checks are important.

"More intense interventions that achieve greater change in activity are needed to confirm these preliminary outcomes," he said. Dr. LeMaster and his colleagues have received funding from the U.S. National Institutes of Health to conduct a follow-up study that will involve working more closely with patients to increase activity.

The study was limited by wide confidence intervals, "so we can only draw preliminary conclusions about the effect of the intervention on foot ulcers," Dr. LeMaster said.

But gradually increasing activity is the key to success for diabetic neuropathy

patients, he said during a question-andanswer session. When asked what clinicians can tell diabetic neuropathy patients about increasing activity, he emphasized using a pedometer to ensure a gradual increase in activity. Ulcers are more likely to occur when someone has been inactive and tries to increase activity too quickly, he said.

In an interview, Prof. Solomon Tesfaye, a consultant physician at the Royal Hallamshire Hospital, Sheffield (England), said that, although regular exercise would clearly be useful in patients with neuropathy, he and his colleagues "have been very cautious in advancing this for fear of foot ulceration.

However, he called the study an "important advance as it reassures us that it is reasonably safe for neuropathic patients to participate in a gradually increasing exercise program if they have appropriate footwear and have received education about how to care for their feet." He cautioned that because the study only included patients without foot ulceration at baseline, he would still advise those with recurrent ulceration "to refrain from excessive walking."

The Feet First study was sponsored by the Robert Wood Johnson Foundation, and the results were published in Physical Therapy (2008;88:1385-98).



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## A Review of Neurology in North America During 2008

BY STEPHEN M. SERGAY, M.B. North American Regional Director, WFN AND RICHARD DESBIENS, M.D. President, Canadian Neurological Society

eurology in North America enjoyed a robust year in 2008 in all areas, from science to advocacy. We are very fortunate to be making progress on many fronts, but research, education, and the practice of neurology continue to be challenged by economic and political forces.

The dynamics of last year's presidential election and the aging populations in the United States and Canada present us with challenges, and we are concerned that we may soon be facing a shortage of neurologists.

### **Report From Canada**

The Canadian Neurological Society (CNS) represents more than 600 neurologists from the 10 provinces and territories of Canada. It is part of the Canadian Neurological Sciences Federation (CNSF), which includes the Canadian Neurosurgical Society, the Canadian Association of Child Neurologists, and the Canadian Society of Clinical Neurophysiologists.

In partnership with the CNSF, the CNS is active in organizing the annual scientific meeting (the Congress) held each June. It provides educational opportunities for its membership in connection with the Maintenance of Certification program of the Royal College of Physicians and Surgeons of Canada. The abstracts and publications derived from the annual meeting, along with abundant peer-reviewed material, are published in the Canadian Journal of Neurological Sciences (www.cjns.org).

The society is also active in advocacy through its branch, the Canadian Brain and Nerve Health Coalition (CBANHC), and through its involvement with the Canadian Medical Association. Canada has a universal access, public-funded health care system, which is challenged by a chronic shortage of doctors and by other factors, such as the aging of the population and inadequate funding. After the release of the CBANHC report in 2007 titled "The Burden of Neurological Diseases, Disorders and Injuries in Canada," the CNS embarked on a study on wait times and access to neurologists throughout Canada.

Our society is active internationally through a program to support neurologists and neurosurgeons from economically underdeveloped countries. After years of support to various countries, we decided to support one country in a more meaningful way: In 2008, we established the Canada-Cuba Partnership, which will help provide physicians with the material and scientific tools they need to continue providing excellent care to their populations.

On the same international note, one of our members, Dr. Vladimir Hachinski, is the first vice president of the World Federation of Neurology.



DR. SERGAY

For more information about the Canadian Neurological Society and the Canadian Neurological Sciences Federation, visit www.ccns.org. Neurologists, neurosurgeons, pediatric neurologists, and clinical neurophysiologists from all over the world are invited to attend our annual scientific meeting in Halifax, N.S., June 9-12, 2009.

### **Report From the United States**

Neurology in the United States is being advanced by a multitude of quality-driven organizations representing neuroscience, neurology education, and neurology care delivery.

The largest of these are the Society for Neuroscience (38,000 members) and the American Academy of Neurology (21,300 members). They are joined by many other organizations that are dedicated to both basic science and care delivery; by adult and pediatric neurology; and, more recently, by increasing numbers of neurology subspecialty organizations, all of which are contributing to the increasing depth and the ongoing dynamism of U.S. neurology.

There are 31 state neurology societies in the United States, which the AAN provides with active support. The Academy also partners with numerous medical and patient organizations.

The annual meeting of the Society for Neuroscience in San Diego, Calif., in November 2007 attracted more than 32,000 attendees. The 60th annual meeting of the American Academy of Neurology in Chicago attracted 12,750 delegates—our new record—consisting mostly of neurologists, 37% of whom work outside the United States.

The AAN offered integrated neuroscience sessions on tropical neurology; new methods of imaging; autism; genetics of epilepsy; stroke imaging and emerging therapeutics; and mitochondrial diseases, among others. Neural repair was the topic of the Future of Neuroscience Conference at the meeting.

As clinical neurology has become increasingly subspecialized, the AAN has supported this process through its member sections.

The AAN also has joined with the other four principal teaching organizations in



**DR. DESBIENS** 

neurology—the American Neurological Association, the Association of the University Professors of Neurology, the Child Neurology Society and Professors of Child Neurology—to form the United Council for Neurologic Subspecialties. The UCNS represents, to date, eight subspecialties, and has accredited 40 subspecialty training programs.

The AAN has recently embarked on a reevaluation of its methods of operation. We are working toward being a more data-driven organization that will react rapidly to change. We conducted a broad and deep examination of the scientific, academic, and professional environment of neurology in the United States to identify opportunities and threats to the success of our work.

Our leadership and staff are committed to meeting these challenges successfully, having built on 60 years of representing neurology in the United States and the following accomplishments of the past 12 months.

► Science. Our science community continues to make great strides in improving our understanding of the basic causes of neurologic disorders. This information is published in many journals throughout the year—to which you are referred—and will not be reviewed here. The AAN and its foundation are providing ever-increasing funding for clinical research training fellowships.

► Education. Despite the advances in neuroscience, only 331 (57.6%) of the 575 PGY-1 and PGY-2 neurology positions offered through the National Resident Matching Program were filled by U.S. allopathic medical school seniors. Perhaps students are threatened by tuition debt, reimbursement patterns, and the demanding nature of the specialty.

The AAN is trying to alleviate these situations both politically and with outreach programs to medical students who are interested in neurology, and courses at the annual meeting that are specifically focused on residents' needs.

More neurologists in the United States are addressing the requirements for Maintenance of Certification mandated by the American Board of Medical Specialties and the American Board of Psychiatry and Neurology (the branch of the ABMS that is focused on neurology).

The American Academy of Neurology offers ABPN-approved educational opportunities at its annual meeting and regional conferences, and an increasing number of online distance learning opportunities, through such tools as the NeuroSAE (Neurology Self-Assessment Examination), virtual annual meeting programs, and the publications Neurology and Continuum: Lifelong Learning in Neurology.

The AAN continues to make Continuum available to all members of the World Federation of Neurology.

▶ Practice and Medical Economics.

Neurologists continue to contend with declining reimbursement, with more than 57% of AAN members reporting decreased compensation for cognitive services since 2000.

This has created so-called "perverse incentives" to spending time with all patients, and more particularly, with those patients who have more complex neurologic problems.

One of the presumed consequences is that over the past decade, more neurologists have moved away from small and solo practices to larger groups. Increasing costs for medical liability insurance contributes to increasing practice costs. Half of the respondents to an AAN/ AMA survey confirmed that in response to these increases, they are making major practice changes, including treating fewer complex cases and discontinuing certain services.

The medical community continues to look for efficiencies that contain within them a greater commitment to quality care, and hopes that electronic health records (EHR) will fill this need. In 2004, former President George Bush set a goal for the majority of U.S. physicians to be using EHRs by 2014; to date, only about a quarter of physicians do so. The AAN continues to assess different EHR platforms, and provides evaluations and additional information to its members.

More neurologists are participating in pay-for-performance and other quality initiatives, which are now required. Much work is necessary, however, to set up the appropriate infrastructure and measurement systems and to confirm their value.

The AAN has worked closely with its members and national organizations, such as the American Medical Association, and, as required, is drafting two measurement sets per year.

Through many of its committees, including the Medical Economics Committee, the Legislative Affairs Committee, and the newly established political action committee BrainPAC, the AAN continues to fight for the rights of patients to access quality neurologic care.

### Continued from previous page

► Advocacy and Health Care Reform. The U.S. health care system is clearly in need of reform. Issues for us include the increasing costs of care, increased numbers of uninsured and underinsured patients, inconsistent access to care, questionable economic incentives, and regional and individual disparities in quality of care. It remains to be seen what type of electoral mandate President Barack Obama receives to change this system.

The AAN members and staff have made significant strides in its advocacy activities. In 2008, it helped lead the way to the elimination of a 10.6% cut in physician reimbursement under Medicare, the government-defined health insurance program.

The main AAN legislative priorities for 2008 have been the following:

▶ Permanent repeal of the sustainable growth rate (that is, the government-derived amount available for physician reimbursement).

Access to imaging services.
Care for veterans with traumatic brain injury.

 Establishment of Epilepsy Centers of Excellence for the Department of Veterans Affairs.
Medical liability reform.

The Academy welcomed the reauthorization of an important children's health insurance plan, the State Children's Health Insurance Program, which was signed by President Barack Obama in early February. Under his tenure, the Academy also looks toward possible removal of restrictions to embryonic stem cell research and reform of the government-run Medicare health insurance program.

The AAN continues to train neurology advocates from its national and international membership. Since 2003, 180 members have received training and are addressing local, regional, and national health care issues. The AAN also continues its annual member visits to Washington, D.C.—known as Neurology on the Hill.

In 2007, the AAN's professional association launched BrainPAC, a political action committee to support federal legislators who champion the concerns of neurologists and patients with neurologic disease.

We celebrated the AAN's 60th anniversary during last year's annual meeting in Chicago, and we are fully engaged in planning to build on this success at our 61st annual meeting. We invite you to Seattle for our 2009 meeting, starting April 25 and running through May 2.

DR. SERGAY is a general neurologist practicing in Tampa, Florida, and president of the American Academy of Neurology. DR. DESBIENS is a researcher at the Hopital de l'Enfant-Jesus in Quebec, Canada.

## World Sleep Day Highlights Dangers of Drowsy Driving

BY ANTONIO CULEBRAS, M.D. Sleep Research Group Chair, WFN, and Cochair of World Sleep Day

he second annual World Sleep Day, an international event aimed at raising awareness of the burden and impact of sleep disorders, will be held on Friday, March 20, 2009. This year, the event will highlight the dangers of drowsy driving. World Sleep Day's message, to "Drive alert, arrive safe," aims to raise awareness that the next-day effects of sleep problems, such as excessive daytime sleepiness and poor concentration, can lead to accidents. World Sleep Day is sponsored by the World Association of Sleep Medicine and endorsed by the Sleep Research Group of the WFN.

Improved diagnosis and treatment of sleep disorders could help to cut fatal or serious road traffic accidents, according to the World Association of Sleep Medicine. Insomnia, one of the most common sleep complaints, has been linked to a significant rise in road traffic accidents, 35% of all accidents are caused by drivers who have not had enough sleep or have not had restorative (quality) sleep. People with insomnia are also up to seven times more likely to be involved in work accidents that cause serious injury or death.

In the United States, 40,000-50,000 people die yearly in traffic accidents, as noted by J. Catesby Ware, Ph.D., chief of the division of sleep medicine at Eastern Virginia Medical School, Norfolk in the United States. Up to 20% of those accidents are thought to be related to fatigue and tiredness.

To help cut the risk of sleepiness while driving, the World Sleep Day message emphasizes the importance of understanding what is needed to ensure alertness when driving. In the words of Dr. Ware, "Just as important as knowing how to get a good night of sleep is learning what it takes to stay awake. These include getting sufficient, quality sleep, having regular bed and rising times, taking regular breaks when driving, and using caffeine judiciously."

Sleep problems constitute a global epidemic that threatens health and quality of life for up to 45% of the world's population. In addition to causing distress to the individual, sleep problems also create a significant burden on society. Sleep apnea, restless legs syndrome, and psychophysiologic insomnia are among the most common alterations of sleep. Paradoxically, research suggests that less than a third of people with moderate to severe sleep problems seek professional help for their sleep problems even though most sleep disorders are preventable or treatable.

Poor quality of sleep or insufficient sleep can also have a negative effect on the health of an individual. In the United States, the direct and indirect costs of insomnia are estimated to amount to \$107.5 billion. Sleep deprivation has been associated with decline in mental health, and people with insomnia are more likely to suffer symptoms of depression and anxiety. Other links have been made between sleep deprivation and conditions such as obesity, diabetes, and weakened immune systems. Insomnia and other sleep disorders can also have a negative impact on overall quality of life and family and social relationships.

The World Sleep Day committee consists of Antonio Culebras, M.D., co-chair; Liborio Parrino, M.D., co-chair; Richard P. Allen, Ph.D.; Sudhansu Chokroverty, M.D.; Christian Guilleminault, M.D.; Claudia Trenkwalder, M.D.; J. Catesby Ware, M.D.; and Allan O'Bryan, Ph.D, executive director.

## **Calendar of International Events**

### 2009

9th International Conference on Alzheimer's and Parkinson's Diseases: Advances, Concepts, and New Challenges March 11-15 Prague www.kenes.com/adpd

5th World Congress of the World Institute of Pain March 13-16 New York www.kenes.com/wip

4th Fred J. Epstein International Symposium on New Horizons in Pediatric Neurology, Neurosurgery, and Neurofibromatosis March 15-19 Eilat, Israel www.fredhorizons.com

24th Conference of Alzheimer's Disease International March 26-28 Singapore www.adi2009.org 2nd International Conference on Psychogenic Movement Disorders and Other Conversion Disorders April 2-4 Washington, D.C.

www.movementdisorders.org/education /pmd

**The Innsbruck Colloquium on Status Epilepticus 2009** April 2-4 Innsbruck, Austria www.innsbruck-SE2009.eu

61st Annual Meeting of the American Academy of Neurology April 25-May 2 Seattle

www.aan.com

21st Annual Symposium on the Treatment of Headaches and Facial Pain April 26

New York www.NYHeadache.com

**6th Baltic Congress of Neurology** (**BALCONE**) May 13-16 Vilnius, Lithuania www.balcone2009.com **1st International Course on Pain Medicine** May 28-31 Granada, Spain www.icpm.net

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### 2010

36th Annual Meeting of the North American Neuro-Ophthalmology Society (Nanos) March 8-12 Tucson, Ariz. www.nanosweb.org

## **Immunotherapy's Emerging Role in Alzheimer's Disease**

BY ANTON P. PORSTEINSSON. M.D. AND KELLY M. COSMAN

esearch into the use of immunotherapy for the treatment of Alzheimer's disease remains vibrant, despite some setbacks.

Bapineuzumab (AAB-001/ELN115727) is a humanized N-terminal monoclonal antibody that has been developed by Elan

Pharmaceuticals Inc. and Wyeth and studied in phase I, II, and III clinical trials. Phase II results were announced recently, and are not without controversy. The phase II study enrolled 234 patients with mild to

moderate Alzheimer's disease (AD), who were infused with placebo or one of four dose levels of bapineuzumab (0.15, 0.5, 1.0, and 2.0 mg/kg) six times at 13-week intervals over 18 months.

Preliminary analyses of the phase II trial found no statistically significant changes on any of the primary or secondary efficacy end points. These analyses also revealed a slightly higher incidence of adverse events in patients treated with bapineuzumab (95%) than in those who received placebo (90%).

Some of the adverse events that occurred with an incidence of greater than 5% in bapineuzumab-treated patients also occurred at more than twice the rate seen in placebo-treated patients. These included back pain, anxiety, vomiting, va-



**DR. PORSTEINSSON** 

#### sogenic edema, hypertension, weight loss, paranoia, skin laceration, gait disturbance, and muscle spasm. The adverse events were reportedly transient and mild to moderate; vasogenic edema was the only seemingly dose-related adverse event.

When the phase II trial results were released, investigators emphasized results from post hoc analyses, which used a

> modified intent-totreat (MITT) repeated measures model that did not assume linearity. They also were adjusted for baseline Mini-Mental State Examination (MMSE) score and stratified according to apolipopro-

tein E4 (apo E4) carrier status.

MITT analyses showed numericalbut statistically insignificant-differences on the subscale of the AD Assessment Scale (ADAS-Cog) and Neuropsychological Test Battery (NTB) that favored the bapineuzumab group in the overall population. In apo E4 noncarriers, the analyses showed statistically significant results on the ADAS-Cog, NTB, MMSE, directional changes on the Disability Assessment of Dementia scale, and the sum of boxes on the Clinical Dementia Rating scale. All of these analyses favored bapineuzumab.

The apo E4 noncarriers also showed statistically significantly less brain volume loss and a smaller, nonsignificant increase in ventricular volume. The analyses of the apo E4 carrier subgroup, however, failed to show statistically significant differences on all efficacy end points except change in ventricular volume; apo E4 carriers taking bapineuzumab actually showed a greater increase in ventricular volume.

The primary notable safety concern resulting from the phase II trial was the occurrence of vasogenic edema (VE). VE developed in 12 patients, all of whom were taking bapineuzumab. The occurrence of VE seemed to be related to dose as well as apo E4 carrier status because 8 of the 12 patients were in the highest dose group and 10 were apo E4 carriers. The investigators reported that VE resolved over time for all patients after discontinuing bapineuzumab. VE did not recur in six patients who were rechallenged with bapineuzumab.

Bapineuzumab has entered into phase III research. Four trials have been initiated since December 2007: two in 200 sites within the United States and Canada, and two in 150 sites in 20 countries outside the United States. Within each pair, one study will enroll 800 apo E4 carriers and the other will enroll 1,250 apo E4 noncarriers. The pairs of studies will follow the same general procedures, except that the apo E4 carrier subgroup in the experimental arm will receive only a 0.5-mg/kg dose of bapineuzumab, whereas the noncarrier treatment group will receive doses at three different levels (0.5, 1.0, or 2.0 mg/kg). Follow-up of the apo E4 genotypes separately, as well as limiting the dose of bapineuzumab for apo E4 carriers, should facilitate better vigilance over safety outcomes. Additionally, the planned separate analyses may improve the chance of detecting a meaningful effect of bapineuzumab in the apo E4 subgroups.

Clinical trials also are progressing with intravenous immunoglobulin, a purified polyclonal antibody product that has been found to block β-amyloid fibril formation or disrupt formation of fibrillar structure. Results from a phase II trial with 24 patients with mild to moderate AD have shown statistically significant improvements on cognitive and global outcome measures that favored immunoglobulin after 9 months continued treatment. Baxter International Inc., maker of intravenous immunoglobulin, is working with the Alzheimer's Disease Cooperative Study to do a phase III trial of this agent.

The monoclonal antibody against  $\beta$ amyloid that has been under investigation by researchers affiliated with Eli Lilly & Co. has also been showing promise of advancing from phase II to phase III research. Following the results of a successful phase II trial of the antibody Lilly has announced its intention to begin a phase III trial in 2009.

DR. PORSTEINSSON is associate professor of psychiatry at the University of Rochester School of Medicine, New York. He reported that his institution receives research support from Elan, Wyeth, Lilly, Pfizer, Merck, Baxter, Toyama Chemical Co., Forest Laboratories Inc., Medivation Inc., GlaxoSmithKline, and Eisai. He is an adviser to Toyama and Medivation and is a speaker for Forest. Ms. COSMAN is the health project coordinator at the school.

## Case Study: Headache and Papilledema in a Young Man

BY REENA S. SHAH. M.D., ROBERT SHIN, M.D., AND LAURA BALCER, M.D.

thin, 27-year-old man pre-Assented with headache, pulsatile tinnitus, and 4 weeks of

transient visual obscurations. General and neurologic exams were normal, except for swelling of the optic disks and peripapillary hemorrhages. Both of the blind spots were enlarged on visual field testing.

> MRI re-Brain

vealed communicating hydrocephalus. His opening pressure was 410 mm H<sub>2</sub>O. Cerebral spinal fluid (CSF) analysis showed RBC 1,170/ mcL, WBC 2/mcL, glucose 81 mg/dL, and protein 235 mg/dL. Spine MRI, including T2-weighted imaging of the lumbar spine, revealed a hyperintense intradural mass at S2, with enhancement on T1-

DR. SHAH

weighted postgadolinium images. After gross total resection, histopathology was consistent with a myxopapillary ependymoma.

This case illustrates an unlikely finding in a young patient with headache, papilledema, and

hydrocephalus: spinal ependymoma. Proposed mechanisms by which spinal tumors may cause hydrocephalus include increased CSF viscosity with decreased CSF flow and absorption; neoplastic inflammatory or arachnoiditis sec-

ondary to hemorrhage or secretion of tumor cells, fibrin, and/or transforming growth factor- $\beta$ ; blockage of the spinal subarachnoid space, reducing the capacity of the CSF reservoir to accommodate large CSF shifts; and compression of spinal venous plexuses, increasing venous intracranial pressure.

Ependymomas are rare neu-



roectodermal tumors, occurring more often in males and in the fourth decade. Most patients have mild symptoms, which may delay diagnosis for years. Standard of care is surgical resection, providing a possibility for

cure. Myxopapillary ependymomas are grade I ependymomas, classically thought to disseminate infrequently, though recent literature has revealed their potential for metastasis. Adjuvant radiation may increase progres-

sion-free survival. The 10-year survival of patients with lumbosacral ependymomas is 94%.

After resection of the tumor, our patient's headaches and papilledema resolved. He remains recurrence free 9 years later. ■

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## **Obituary: Dr. Raymond D. Adams**

### BY ALLAN H. ROPPER, M.D.

ur colleague Dr. Raymond D. Adams died at age 97 in September last year. For his American and international friends, his passing marks the end of a golden era in neurology in which the breadth of his personal and professional relationships gave rise to major advances in neuropathology and clinical neurology.

Dr. Adams was born in Portland, Oregon, in 1911 and attended the University of Oregon and Duke University School of Medicine in Durham, North Carolina. He trained as a resident in both neurology and psychiatry and obtained one of the first of the Rockefeller Fellowships for advanced experience in these fields. After a post at the Tufts Medical School and the Pratt Diagnostic Hospital in Boston, he spent 5 years as an assistant pathologist at Boston City Hospital and the Mallory Institute of Pathology.

At Boston City, he encountered one of the lions of the field, Dr. Derek Denny-Brown and observed his work carefully. Although he was reluctant to criticize Dr. Denny-Brown's approach, he determined from that experience to set out on his own program by avoiding Sherringtonian physiology in favor of neuropathology. Dr. Adams saw an opportunity to study the deep details of

### HE WAS ONE OF THE FEW IN THE FIELD WHO DISPLAYED THE SCIENTIFIC AND CLINICAL ATTRIBUTES OF THE REFINED, INTELLECTUAL PHYSICIANS OF THE PAST.

neurologic disease through the emerging techniques of histopathology and experimental pathology, and over the following 45 years, he influenced virtually every corner of neurology.

His work extended from the development of the models for experimental autoimmune encephalitis and experimental autoimmune neuritis with Byron Waksman, to the clinical and pathological description of numerous muscle diseases with Person, Banker, Kakulas, Samaha, and John Walton, including what is now called inclusion body myositis.

His name is attached to myoclonus after anoxic brain damage with James W. Lance, and he was a chief participant in defining normal pressure hydrocephalus with C. Miller Fisher and Soloman Hakim, transient global amnesia, the neuropathology of multiple sclerosis, basilar artery stroke, Guillain-Barré syndrome and diabetic nerve infarction with Arthur Asbury, oculopharyngeal dystrophy (also with an eponym that includes his name), childhood metabolic diseases with Gilles Lyon, Philip Dodge, and Hugo Moser, developmental disorders with Guy McKhann and Edwin Kolodny, and deficiency and alcohol diseases of the nervous system with Roy Swank and Maurice Victor.

Dr. Adams can be properly credited with formulating the modern clinical criteria for brain death while serving on the Beecher (Harvard) committee to study irreversible coma. His books on neurosyphilis, pathology of the nervous system, muscle diseases, and metabolic diseases of childhood stand as unusually lucid expositions by a master intellect and observant physician.

His extreme lucidity allowed him to provide both analytic and synthetic perspectives on almost any topic in neurology. His beautiful Thursday Grand Rounds, almost always accompanied by examination of an ill patient, simulated his writing in its clarity and turn of phrase. He wished to understand "the whole story" and reached back to Sir Gordon Holmes, Guillaume Duchenne, Sir Charles Symonds, Jacques Jean Lhermitte, and Charcot when necessary. He was one of the few individuals in the field who displayed the broad scientific and clinical attributes of the refined and intellectual physicians who were in the past an essential part of the Academy.

From the time of his early training in psychology at the University of Oregon, he maintained a lively interest in the field. He expressed great respect for the first chief of psychiatry at Massachusetts General Hospital, Dr. Stanley Cobb, and told warm and humorous stories of their long conversations. His insistence on understanding psychiatric diseases as core neurologic phenomena is reflected by their inclusion in his writings and a great curiosity about human nature. He absorbed William James and the early American and European psychologists but acquired strong positions regarding psychoanalysis and the tendentiousness of the Boston psychiatric community.

Publishing more than 250 original papers and seven monographs, he is perhaps most widely known for his chapters in the early editions of Harrison's Principles of Internal Medicine that subsequently became the basis for his opus, Principles of Neurology. That book, written with his close colleague Maurice Victor changed pedagogy in the field by presenting the basic anatomical, physiologic, and pathologic principles of neurology and juxtaposing them with authors' authoritative clinical experience. It remains one of the very few medical works of extensive scope given by a unitary voice and style. Dr. Adams had a marvelous command of the language and shared with Dr. Victor considerable literary skill and a desire to make his writings readable by a broad audience of intelligent people.

In addition to his long-standing appointment as Bullard Professor of Neuropathology at Harvard Medical School and as chairman of the Department of Neurology at Massachusetts General Hospital, he founded and served as director of the Kennedy research laboratories and the Shriver Center for Mental Retardation at the storied Walter E. Fernald Developmental Center in Waltham, Massachusetts.



For almost 50 years, Dr. Raymond D. Adams presided over major advances in neuropathology and clinical neurology.

He was appointed to the faculties of the American University of Beirut, Lebanon; Karolinska University Hospital in Stockholm; and l'Hôpital Cantonal de Lausanne, Switzerland; and he held eight honorary degrees from various international institutions and societies. He was a former president of the American Neurological Association and the American Neuropathology Society. Medals or meritorious honors were bestowed by the Neurologic Societies of Lebanon, Brazil, Great Britain, Switzerland, Germany, Columbia, Australia, Greece, Belgium, and Argentina.

Dr. Adams's international credentials were rooted in a familiarity with many of the great neurologists and neuropathologists of his time and the selftaught ability to read the early neurological literature in German and French. In his later years, he enjoyed reading a native French novel before going to bed. He had established a close relationship with the American University of Beirut, to which he donated a portion of his personal library and where he lectured on a regular basis. He met his second wife, Dr. Maria Salam-Adams, through that association.

Dr. Adams can appropriately be credited with altering the dimensions of American neurology, not only by being the progenitor of more than a dozen department chairmen, but also by bringing into the circle of neurology the study of diseases of muscle, development of the nervous system, mental retardation, and the neurological manifestation of medical disorders including in the connective tissue diseases, diabetes, hepatic encephalopathy, vitamin and nutritional deficiencies, and many others. He initiated studies of genetic and developmental neurological diseases in the experimental neuropathology division at Harvard Medical School. Through foresight, he cultivated early on sections in his department at Massachusetts General on language problems of children, myasthenia gravis, immune diseases and multiple sclerosis, epidemiology, stroke, and infectious diseases of the nervous system, almost all built by gently guiding his own residents to take a special interest in a new field.

An upstanding, very modest, and sometimes formal but not officious individual, Dr. Adams was held in extremely high regard by his residents and by leaders in other fields of medicine. He had great natural respect for the prominent internists of his time and generously shared his many insights with them.

One of his outstanding personal characteristics was loyalty to those around him, and he particularly valued his daily interactions with Dr. C. Miller Fisher and Dr. E.P. Richardson, who, together with him, formed the most identifiable individuals in the Massachusetts General department of neurology.

At yearly departmental holiday events, he highlighted the importance of educating the next generation of residents and spoke of the interdependence of the staff and trainees. To that end, he maintained that a full education in neurology included hands-on clinical training in psychiatry and neurosurgery, not to mention his beloved year of neuropathology, during which neurology residents removed, fixed, blocked, and signed out all the brains.

Beyond the discursive details of what is perhaps the most accomplished neurological career of the 20th century, Dr. Adams was a fatherly mentor and became as he aged a genuinely warm and no-nonsense friend. At the age of 94, he was still engaging in polemical discussions about the validity of diffuse axonal injury, his views of the development of the molecular understanding of muscular dystrophy, and less-accustomed judgmental views of modern psychiatry. He actively edited portions of the eighth edition of Principles of Neurology at age 91.

His numerous trainees and colleagues are saddened by his death but grateful for his enormous productivity and friendship. He leaves a broad and accomplished family including Nina, his stepdaughter; Iga, his sister-in-law; his eldest son Bill, a prominent educator; three daughters; 11 grandchildren; and 16 great-grandchildren. A memorial service will be held in Boston in 2009.

DR. ROPPER is in the department of neurology at the Brigham and Women's Hospital and lectures in neurology at Harvard Medical School, Boston.

## **Trustee Profile: Johan A. Aarli**

BY JOHAN A. AARLI. M.D.

t the Council of Delegates meeting held in 2005 in Sydney, I was elected President of the World Federation of Neurology. As First Vice President, I had been the WFN liaison officer to the World Health Organization. There, I expanded my appreciation of the importance of public health in neurology. I also gained an appreciation for the dramatic health care crisis in sub-Saharan Africa, one of the world's poorest regions. My priority, therefore, is to promote neurology in developing countries, particularly in Africa, and I have the great honor to work in a team that realizes the importance of and works for the "Africa initiative."

My career in neurology began in the 1960s, a period marked by dramatic changes in treatment procedures. Before that time, neurology was a discipline with a reputation for advanced clinical diagnosis but no therapeutic possibilities. Ours was the first generation of neurologists who experienced the awakening effects of L-dopa in Parkinson's disease. New antiepileptic drugs were introduced, and freedom from pain in trigeminal neuralgia could be obtained without dramatic neurosurgical intervention. I became a certified specialist in neurology in 1968.

This also was an era when immunology entered neurology. Neither thymectomy nor steroid treatment was a generally accepted therapeutic modality in myasthenia gravis. I defended my PhD thesis in 1972, demonstrating antibodies to an extractable striated muscle antigen. At that time, antibodies to acetylcholine receptor

had hardly been demonstrated in human disease. I did research on experimental myasthenia gravis with Edith Heilbronn at the National Research Institute of Sweden in Stockholm and, during a sabbatical at Dr. Barry Arnason's department at the University of Chicago, I showed that titin is the striatal muscle antigen to which most patients with thymoma and myasthenia gravis have antibodies.

For a neurologist with an interest in immunology, it was impossible not to become fascinated by the pathogenesis of multiple sclerosis. In 1973, I worked at Leeds (England) University with Prof. Charles Lumsden, the leading multiple sclerosis pathologist at that time. He believed multiple sclerosis was an autoimmune disorder related to the presence of antibodies to myelin. Together with the electron microscopist Samuel Aparicio, we showed that what were believed to be antibodies to myelin protein as demonstrated by immunofluorescence was in actuality nonspecific binding by the Fc part of the immunoglobulin G molecule.

The World Congress of Immunology was held in Brighton in 1973 and had two workshops of interest for neurologists: One was on myasthenia gravis, and the other was on immunologic aspects of neurologic disorders. We were a group of young men who met in Brighton: Barry Arnason, Oded Abramsky, Dale McFarlin (deceased), and Robert P. Lisak. We have since remained close friends.

In 1977, I became professor of neurology and head of the department of neurology at the University of Bergen (Norway) Hospital, where I remained

Child & Family Research Institute



Dr. Aarli's groundbreaking research explored the role of immunology in neurologic disorders.

until retiring in 2006. During that time, I had the great opportunity to gather young, hard-working neurologists with special competence in a variety of sectors of neurology. Together, we established a spinal unit, a regional epilepsy center, an amyotrophic lateral sclerosis clinic, a stroke unit, a national multiple sclerosis center and registry, a myasthenia gravis competence center, and a neuroimmunology research center. Our department was a central feature of the university hospital. In 1996, I was knighted by King Harald V to Knight, First Class, of Saint Olav's Order.

I was vice dean of the faculty of medicine at the University of Bergen from 1982 to 1984, dean from 1985 to 1987, and chair of the Board of University Research Bergen UNIFOB from 1989 to 1993.

I also was chairman of the Norwegian Neurological Association from 1984 to 1988 and am now an honorary member.

I am also an honorary corresponding member of the American Academy of Neurology, as well as honorary foreign member of the Association of British Neurologists and of the French Society of Neurology.

The European Federation of Neurological Societies (EFNS) was founded in 1991 by Frantz Gerstenbrand. Its growth almost explosive, and this time was a fascinating period for European neurologists. As the Norwegian delegate, I was elected chair of the liaison committee from 1991 to 1995. Thereafter, I had the great honor to be the

chair of the Teaching Course Committee for three periods, from 1997 to 2003, followed by 2 years as the Secretary-General of EFNS.

I became the Norwegian delegate to WFN in 1991, and in 1995, John Walton invited me to chair the WFN Public Relations Committee. Under the administrations of James Toole and Jun Kimura, I was responsible for contact with World Health Organization.

My wife Gullborg and I were married in 1962, and we have 5 children and 14 grandchildren. Two sons and one son-inlaw are physicians. When we are not traveling, Gullborg and I love to stay at the family summer home, a farm in the unspoiled mountains of southern Norway. My favorite interests include history and literature, and I am an active founding member of the Norwegian Neuroliterary Club and of the Norwegian Thomas Mann Academy.







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