

# WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

## AOCN-IANCON Hosts 1,085 Delegates

BY M.M.  
MEHNDIRATTA, M.D.

The 12th Asian Oceanian Congress of Neurology and 16th Annual Conference of the Indian Academy of Neurology, held in New Delhi Oct. 23-26, 2008, went very well.

The congress had 1,085 delegates in attendance, of which 903 were from India and 282 were from Australia, Bangladesh, Belgium, Chile, Canada, China, Croatia, the Czech Republic, Dubai, Germany, Hong Kong, Indonesia, Israel, Japan, Malaysia, Manila, Morocco, New Zealand, Norway, Nigeria, Pakistan, Panama, Philippines, the Russian Federation, Singapore, South Korea, Sri Lanka, Switzerland, Taiwan, Thailand, the United Kingdom, and the United States.

There were 30 international advisers from different countries of the Asian Oceanian region and 27 national advisers.

The four simultaneous pre-conference workshops were on EEG (177 delegates), multiple sclerosis (78 delegates), movement disorders (57 delegates), and advocacy (21 delegates). These informative workshops were held at the India Habitat Center.

This was the first time an advocacy workshop had been organized in India.

Because we in our profession



Dr. M.M. Mehndiratta, organizing secretary of AOCN-IANCON 2008, addresses the delegates, who hailed from 33 countries.

all are advocates in one way or the other, the workshop was organized to further the cause of our patients and our profession with the media, administrators, and politicians.

Our aim was to make diagnostic and therapeutic measures readily available in various neurologic departments, at reasonable cost.

It was indeed an honor for all of us at the Indian Academy of Neurology and Asian Oceanian Association of Neurology to welcome very distinguished faculty members (and patrons for our conference) such as Dr. Jo-

han A. Aarli, president of the World Federation of Neurology; Dr. Stephen M. Sergay, president of the American Academy of Neurology; Dr. Amado San Luis, president of the Asian Oceanian Association of Neurology; Dr. Michael Finkel, president of the World Neurology Foundation; Dr. Mark Hallett, editor of *WORLD NEUROLOGY*; and Dr. Niphon Pongvarin, the chief organizer of the World Congress of Neurology 2009.

It was a matter of great honor for all of us that His Excellency Dr. A.P.J. Abdul Kalam, the former president (People's Presi-

dent) of India, inaugurated the conference. The abstract book was released by Dr. Aarli; the Scientific Program was released by Dr. Sergay.

An international group of 20 senior teachers was recognized for their services and achievements in neurology. The certificates of appreciation were given by Dr. Kalam. The Continuing Medical Education was inaugurated by Dr. J.S. Chopra who had been the editor of *WORLD NEUROLOGY* for 8 years.

CME was divided into two sessions, one on geriatric neurology and one on pediatric neurology. The sessions were of the highest standard and were very well received.

There were 251 presentations made under the poster and platform sessions. Awards were given to the four best papers.

There were four orations, the details of which are as follows:

- ▶ Dr. San Luis gave the Indian Academy of Neurology Oration: End of Life Care in Acute Severe Stroke.
- ▶ Dr. Aarli gave the N.H. Wadia Oration: World Federation of Neurology at a Crossroads.
- ▶ Dr. Madhuri Behari, President of the Indian Academy of Neurology, gave the Presidential Oration: Shuffling Along and More.

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## Comorbidities Delay Diagnosis in Multiple Sclerosis

BY ELIZABETH  
MECHCATIE

Elsevier Global Medical News

Obesity, smoking, and physical and mental comorbidities delayed the diagnosis of multiple sclerosis and were associated with a greater degree of disability at the time of diagnosis in a study of nearly 9,000 individuals enrolled in a multiple sclerosis registry.

The results "suggest that practitioners treating persons with chronic diseases should not attribute new neurologic signs or symptoms to existing conditions without careful consideration," wrote Dr. Ruth Ann Marrie of

the University of Manitoba, Winnipeg, in *Neurology* (doi:10.1212/01.wnl.0000333252.78173.5f).

Calling on 2006 data from the North American Research Committee on Multiple Sclerosis Registry, the study's researchers compared the duration between symptom onset and multiple sclerosis diagnosis in patients both with and without vascular, musculoskeletal, mental, and other types of comorbidities.

The presence of obesity or smoking, or the presence of physical or mental comorbidities delayed the diagnosis by a mean of 7 years, after adjustment for demographic and clinical characteristics, the authors found.

During an interview with *WORLD NEUROLOGY*, Dr. Trygve Holmøy, who was not involved with the current study, commented: "Given the mounting evidence that early treatment of multiple sclerosis is beneficial, the traditional view that a prolonged diagnostic delay in multiple sclerosis is acceptable or even desirable can no longer be sustained."

For example, he said, "Studies have shown that treatment with [interferon-beta] and glatiramer acetate delay the time to the second clinical attack in patients with the first clinical event suggestive of multiple sclerosis."

Certain immunosuppressive

drugs, such as alemtuzumab, also have been shown more effective when started early, added Dr. Holmøy, who is a consultant neurologist at Ullevål University Hospital, Oslo, Norway.

The study findings are particularly alarming in light of the high

rate of disability found in this study population.

"More than 50% of the newly diagnosed patients reported overweight or obesity," observed Dr. Holmøy.

"And 22.6% reported vascular

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#### From Italy:

Toxins 2008, which took place in Baveno this past summer, shows that this exciting field is still evolving.

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#### From Morocco:

In this African nation, site of the World Congress of Neurology 2011, neurologists share 100 CT scanners for 33 million people.

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#### From Uruguay:

Delayed access to drugs hasn't dampened the enthusiasm and sense of camaraderie among practitioners in this nation.

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## EDITOR IN CHIEF'S COLUMN

# Psychogenic Disorders

Every time I go to the clinic, I am more concerned about patients with psychogenic disease—specifically, psychogenic movement disorders. The most common are patients with psychogenic nonepileptic seizures, but there are also those with psychogenic weakness, sensory loss, blindness, aphonia, and memory loss. Psychiatrically, they fall mostly into the category of somatoform disorder, somatization, or conversion, but we really do not understand the pathophysiology. Anxiety and depression are common, but their role in psychogenic disorders is not certain.

About 20% of the patients in my practice have psychogenic disorders. But the usual estimate is closer to about 10% in an average practice. The patients are often misdiagnosed, and even

when correctly diagnosed, resist. They would rather have a brain tumor than a psychiatric condition. They often do have a significant problem; many are very disabled. It is important to be clear that these patients have a “real” disorder; saying that it is not real just confuses the situation (and the patient).



BY MARK HALLETT, M.D.

A psychogenic disorder can be called functional or nonorganic, but it is very real to the patient and in terms of symptoms. For example, if a limb is shaking, regardless of cause, it is a real tremor.

While most patients with psychogenic disease have somatization or conversion disorder, a few are malingering. These patients are lying, saying that the movement is involuntary, when it is actually voluntary. Unfortunately, we cannot identify them easily, since we have a difficult time telling

when someone is lying. It has been estimated that in the United States, somatization is responsible for 10%-20% of all office visits, a large number of emergency room visits, many unnecessary tests, and about 16% of all health care expenditures, costing about \$256 billion dollars per year (Arch. Gen. Psychiatry 2005;62:903-10).

While we often find this a difficult diagnosis, at times we can make it with certainty. There are some clinical clues, such as when the movement goes away with distraction or a tremor synchronizes with voluntary tapping at different frequencies.

These patients often need psychiatric help, but it is frequently difficult to find such help. Psychiatrists are not often knowledgeable about psychogenic neurologic disorders, and even if they were, they are often not in a position to be helpful. It is likely that these patients need long periods of psychotherapy, and the reimbursement system (at least in

the United States) does not pay very well for doctors to spend time talking to patients.

The pathophysiology of psychogenic disease needs to be identified to design better therapies. But knowing the cause will also be valuable to understand the pathophysiology for its own sake. It will be fascinating to find out how movements that look so voluntary are not.

This may help us to understand what it means for a movement to be perceived as voluntary. Psychogenic disease may well provide an important clue to one of the challenging problems of physiology and philosophy.

Many of these problems and issues will be discussed at the upcoming Second International Symposium on Psychogenic Movement Disorders and Other Conversion Disorders in Washington, April 2-4, 2009.

I hope we can make more progress in this frequent, challenging, and important condition. ■

## Headquarters Has Moved

WFN Headquarters Office has moved to more modern premises after 10 years in the historic Medical Society of London building on Chandos Street in London.

The new home is in Richmond-upon-Thames, easily accessible to central London and from Heathrow airport. In addition to better office facilities and electronic communication, the new offices also include a meeting room.

The new mailing address is Hill House, Heron Square, Richmond, Surrey, TW9 1EP, UK.

The telephone numbers are +44 (0)208 439 9556/9557; the fax is +44 (0) 208 439



WORLD FEDERATION OF NEUROLOGY

9499. The WFN's new e-mail address is [info@wfneurology.org](mailto:info@wfneurology.org). ■

## World Federation of Neurology Site and World Congress Site Now Updated

Both the 19th World Congress and the World Federation of Neurology Web sites have been updated. On the Congress site, at [www.wcn2009bangkok.com](http://www.wcn2009bangkok.com), information is now available regarding the preliminary program and general information about the Congress, to be held in Bangkok Oct. 24-30, 2009. The updated World Federation of Neurology Web site, [www.wfneurology.org](http://www.wfneurology.org), features an inviting, easy-to-use design. ■



WWW.WCN2009BANGKOK.COM

The World Federation of Neurology Web site is now updated. Add it to your list of favorite sites, and check back often at [www.wfneurology.org](http://www.wfneurology.org). ■



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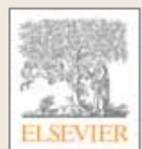
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## THE PRESIDENT'S COLUMN

## WFN, World Health Organization Have Similar Missions

In October this year, World Health Organization Director-General Margaret Chan introduced the WHO Mental Health Gap Action Program (mhGAP), pointing out the need to scale up medical services for mental, neurologic, and substance use disorders. The program is especially designed for low- and lower-middle-income countries. By doing this, WHO has taken an important step to show its responsibility for the global burden of neurologic disorders. It is time to appreciate the magnitude of that burden.

WHO programs, projects, and activities in the areas of mental and neurologic disorders are closely linked. In many ways, that link began with the Global Burden of Disease study, an international collaborative project among WHO, the World Bank, and the Harvard School of Public Health, Boston. Their report produced evidence that the impact of neurologic disorders on global health had previously been underestimated. It identified neurologic disorders as one of the greatest international threats to public health.

The burden of noncommunicable dis-

eases now accounts for nearly half of the global burden of disease. Also in low- and middle-income countries, almost 45% of the adult disease burden globally now is attributable to noncommunicable disease. An aging population and changes in the distribution of risk factors have accelerated the noncommunicable disease share of total disease burden in many developing countries.



BY JOHAN A. AARLI, M.D.

The WHO Program on Neurologic Disorders and Neuroscience focused on disorders that are of public health importance because they are frequent; they cause substantial disability; and they create a burden on individuals, families, communities, and societies all over

the world.

They comprise epilepsy, headache, dementing disorders, multiple sclerosis, Parkinson's disease and related disorders, stroke, pain syndromes, and brain injury. WHO has stated that neurologic services should be provided at all levels of health care, and especially in primary care settings, which is where most patients with neurologic disorders receive treatment. This was clearly pointed out in the

WHO/WFN report, "Neurologic Disorders: Public Health Challenges," which was published last year.

With that publication, WHO recognized neurologic disorders as a public health problem of great magnitude, which should be brought to the attention of health planners and administrators. A 2005 report, "Atlas: Country Resources for Neurologic Disorders," made it clear that there is a critical shortage of neurologists in many parts of the world. This deprives a large proportion of people neurologic care, particularly those who are economically challenged and living in remote and rural areas.

In fact, the prevalence of neurologic disorders is highest in rural areas. Until training programs have been upgraded, it is of utmost importance that patients with neurologic disorders who live far away from centers of neurologic knowledge are treated by primary care.

In India, Prof. Gourie-Devi has signaled health care delivery through rural community health centers offering close interaction with specialist neurologists in tertiary institutes.

We need a comprehensive system of neurologic care at the primary level. Training primary health care workers to diagnose and manage common and treat-

able neurologic disorders (such as epilepsy, stroke, migraine, peripheral neuropathy, Parkinson's disease, etc.) will be essential, and could form the backbone of national programs for neurologic care.

Fifty years ago, the founders of the World Federation of Neurology declared

**WHO HAS STATED THAT NEUROLOGIC SERVICES SHOULD BE PROVIDED AT ALL LEVELS OF HEALTH CARE, ESPECIALLY IN THE PRIMARY CARE SETTING.**

that part of its mission is to enable colleagues in the third world to improve services and promote high standards of neurologic medicine.

Difficulties in the integration of neurology into primary health service have remained a barrier, especially in lower income nations. However, the signals from Geneva may represent a challenge to health administrators to overcome those obstacles. ■

## HIGHLIGHTS FROM THE JOURNAL OF NEUROLOGICAL SCIENCES

## Early Onset of Sporadic ALS in Tropical Regions

Amyotrophic lateral sclerosis (ALS) is a relentlessly progressive degenerative disease of the motor neurons, both upper and lower. It is incurable and only minimally treatable. It is seen in both genders and in all parts of the world.

Apart from a few fascinating exceptions, it is generally uniformly geographically distributed. The disease usually leads to death within a few years.

The disease is highly variable and can have many different presentations, progressing slowly or rapidly, beginning in the legs or arms or bulbar muscles, and exhibiting more upper than lower motor neuron involvement or vice versa.

ALS involves only motor function; sensory and autonomic neurons are spared. The disease may confine itself to a single extremity (usually an arm in the monomelic form) and progress no further. Alternatively, the disease can skip from brainstem to spinal cord or from one extremity to another. It can occur sporadically or be autosomal dominant in about 10% of cases.

The cause of the sporadic form of the disease, the most common type, is unknown but probably involves multifactorial with polygenic and environmental contributions.

The known environmental factors that can affect motor neurons include neurotoxins and viral infections. An example of the former is improperly processed neurotoxic foodstuffs such as cycad seeds, which have been implicated in the ALS-parkinsonism-dementia complex of Guam. As for the latter, viral infections affecting both upper and lower motor neurons are not rare and include flaviviruses such as Japanese encephalitis, some of the tick-borne encephalitides, and West Nile virus.



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

Some cases of human motor neuron disease have been ascribed to retroviruses as well.

Epidemiologic studies can be difficult to carry out over large populations over long periods of time. Nevertheless, such studies can be crucial in suggesting broad categories of causality.

In this very interesting paper, the investigators gathered data on 1,153 patients with sporadic ALS who were referred to their tertiary medical center, and characterized them extensively in a cross-sectional manner.

They tabulated the gender, age at onset of disease, distribution of the initial deficits, clinical and electromyographic findings, and survival, and these data are well summarized in the paper (J. Neurol.

Sci. 2008;272:60-70).

In an intriguing analysis, the authors compared their data with those of other studies that were conducted in developing countries in Africa and the Indian subcontinent, as well as from studies performed in North America and Britain.

A consistent trend was found that their patients, like those in other tropical areas, had a younger age of ALS onset and longer survival after onset. That this is at

**PATIENTS IN TROPICAL AREAS HAD A YOUNGER AGE OF ALS ONSET AND LONGER SURVIVAL AFTER ONSET.**

least in part due to environmental causes is suggested by the consistency of these results across different racial/ethnic groups in the tropics.

This type of observation, if true, has important implications about the pathogenesis of the disease, and data such as reported here provide a rich source of hypothesis generation.

Dr. A. Nalini, the first author of this paper, is currently additional professor at the National Institute of Mental and Neuro-

sciences, Bangalore, India, which is a national referral center for neurologic disorders.

As a medical student at Bangalore Medical College, Dr. Nalini found neurology to be challenging and completed her neurology training in 1994. She wrote her thesis on a trial of cyclophosphamide in motor neuron disease, under the guidance of Prof. M. Gourie-Devi.

Since 1989, Dr. Nalini has continued to work on motor neuron disease and its variants like monomelic amyotrophy and Madras motor neuron disease. "My future work would continue on starting certain multicenter drug trials in ALS and also ... on the genetics of the enigmatic diseases of Madras motor neuron disease and monomelic amyotrophy."

Dr. Nalini is also interested in primary muscle diseases and conducts the multidisciplinary neuromuscular disorders clinic at the Institute.

A particular strength of the Institute is the access to a large, well-characterized clinical population. "As we have the strength of immense patient population I concentrate on studying the clinical pattern of these disorders among our patients and hence shall continue to write clinical articles." ■

DR. TSELIS is an associate professor of neurology at Wayne State University, Detroit, Mich. U.S.A., and is the book review editor for the *Journal of the Neurological Sciences*.

# Toxins 2008 Shows Field Is Still Evolving

## Data provide new interpretations on the efficacy of botulinum toxins for CNS disorders.

The international conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins (Toxins 2008) took place in Baveno (Lake Maggiore, Italy) on June 12-14, 2008. As many as 734 delegates from 43 countries attended to discuss the latest developments in fundamental knowledge and clinical applications.

Although the mechanisms by which different botulinum toxin serotypes operate have been elucidated, new knowledge about many aspects related to their functioning, biologic activity, and clinical use is increasing.

The subject of one lively controversy related to the possibility that botulinum toxins may influence the central nervous system by direct transneuronal transport, similar to the mechanism of tetanus toxins. To this end, Dr. M. Caleo from Consiglio Nazionale delle Ricerche, Pisa (Italy), who published a highly cited set of experiments on the long-distance retrograde effects of type A botulinum toxin (J. Neurosci. 2008;28:3689), pre-

sented a lecture that was then critically analyzed by Dr. Oliver Dolly from Dublin City University.

The general conclusion seemed to be that these animal experiments are of high interest but have no implications for the safety of botulinum toxin used in current clinical practice.

The data provide new interpretations on the efficacy of botulinum toxins for the treatment of central nervous system disorders, such as dystonia or spasticity, according to Dr. Dolly.

In another highly attended session, four representatives of the manufacturers of botulinum toxin products, which are licensed for clinical use, discussed the "unique properties" of their branded products. This direct comparison generated a spirited discussion that highlighted similarities and differences among these products. Prof. Ryuji Kaji from University of Tokushima (Japan) reported on the efficacy of a new toxin produced in a public laboratory in Japan that is not yet commercially available.

Thematic sessions dealt with dystonia, spasticity, autonomic and cosmetic applications, pain syndromes, and future developments.

Structure-function relationships were the object of two dedicated sessions. There is increasing expectation of the possibility of the development of new molecules for specific clinical applications (e.g., with increased specificity for sensory or motor neurons).

A way to explore the future is through the production of chimeras, as discussed in a plenary session at Toxins 2008.

Immune factors influencing the activity and efficacy of botulinum toxins were the subject of another session. This topic has been abundantly discussed during the past years and remains an issue of debate.

Over 150 posters were presented in Baveno. They provided a focus for interaction and discussion on subjects spanning from the fundamental mechanisms of toxin actions to potentially novel clinical indications. The poster sessions at lunchtime

were highly attended.

By the meeting's conclusion, it was clear that this is still an active and evolving field, with new developments to come both in fundamental knowledge and in clinical applications.

Botulinum toxins have become a well-accepted medication in the clinical practice of neurology, with a high number of indications and potential future indications. The pioneering times of surprise and discovery are now over: As fundamental knowledge progresses, clinical applications will be systematized into evidence-based focused protocols.

The next meeting, due to take place in the United States in 2010 or 2011, will take into account the future developments in this exciting field. ■



BY ALBERTO ALBANESE, M.D.

DR. ALBANESE is a neurologist at the Istituto Nazionale Neurologico of the Università Cattolica del Sacro Cuore in Milan, Italy. He was chairman of the scientific committee for Toxins 2008.

# BoNT for Headache: What You Need to Know

The therapeutics and technology assessment subcommittee of the American Academy of Neurology recently published an evidence-based review of the safety and efficacy of botulinum neurotoxin (BoNT) in the treatment of autonomic and urologic disorders and low back and head pain (Neurology 2008;70:1707-14). This was based on a literature search for therapeutic articles relevant to BoNT. Conclusions and recommendations were developed based on the highest level of evidence and put into current clinical context. While clinicians' practice may suggest stronger recommendations in some of these indications, evidence-based conclusions are limited by the availability of data.



BY STEPHEN D. SILBERSTEIN, M.D.

The subcommittee recommended:

- ▶ Based on published class I and class II studies, BoNT injection probably is ineffective in the treatment of episodic migraine (EM) (level B).
- ▶ Based on inconsistent results from four class II studies, there is insufficient evidence to support or refute a benefit of BoNT for the treatment of chronic daily headache (CDH) (level U).
- ▶ BoNT injections should not be considered in patients with EM and chronic tension-type headaches (CTTH) (level B).

### What Does This Mean?

Basic science data and clinical experience support a beneficial effect of BoNT in the treatment of some types of headache. However, data from clinical trials are inconclusive (for CDH) or negative (for EM

and CTTH). What are the reasons for this discrepancy?

### Patient-Related Factors

Patients who described their head pain as pressure from outside ("imploding headache") or as a feeling of eye popping, responded better to BoNT, compared with those patients who described their pain as pressure from inside ("exploding headache") (Pain 2006; 125:286-95). Mathew et al. looked at predictors of response to botulinum toxin type A (BoNT-A) in 82 CDH patients, most of whom had chronic migraine (CM) (Headache 2008;48:194-200). Predictors of response to BoNT in CM patients were unilateral headache, scalp allodynia, and pericranial muscle tenderness.

These findings may help select patients who will be most likely to respond to BoNT in future studies and in clinical practice:

- ▶ CDH patients with disease duration greater than 30 years may be less likely to respond to BoNT-A than are those with a shorter disease duration (Headache 2005;45:308-14). In the controlled trials, patients with a wide range of disease duration were included and, in some studies, the duration was not specified. Selecting patients with shorter disease duration may therefore result in a more robust positive effect of botulinum neurotoxin on headache.
- ▶ Patients who do not use concurrent headache preventive drugs may do better after BoNT treatment, compared with

those patients who do (Headache 2005;45:315-24). The placebo response rate in the BoNT studies was high, and reached 50% or more in some studies. What are the predictors of placebo response in patients who participated in a controlled study of BoNT for migraine (Cephalalgia 2007;27:528-34)? Male gender, history of opioid use, and injections in the neck/shoulders were associated with placebo response. These findings may have implications for the design of future studies.

- ▶ Patients with CDH who are overusing pain medications often need to be detoxified as part of successful headache treatment. However, a recent retrospective study showed that patients with CDH who overused pain medications responded as favorably to BoNT-A treatment than those who did not (Headache 2005;45:825[abstract]).

### Study Design Factors

What should the outcome be for CDH trials? Does a mild headache that lasts 1 hour have the same real-life impact as a moderate to severe headache that lasts more than 4 hours? In many of the trials, the primary outcome measure was the decrease from baseline in headache frequency, regardless of severity.

The International Headache Society has recommended an analysis of moderate to severe headaches of a duration of at least 4 hours. Applied retrospectively, it allowed BoNT-A to be separated from placebo.

### Treatment-Related Factors

The optimal way to administer BoNT-A for headache prevention ("fixed dose" or "follow the pain"—or a combination of

both) has not been determined. In the studies done so far, different approaches and different doses were used, possibly contributing to discrepancies in the results. Many believe that the combination is best.

Clinical experience suggests that BoNT-A is effective for some headache patients. However, the results of exploratory studies so far have been inconclusive (for CDH) or negative (for EM and CTTH). BoNT-A may be effective for specific subgroups of CDH patients (for example, patients who do not use concurrent preventive medications).

Although current data do not support the use of BoNT for the treatment of all patients with episodic migraine, specific subgroups of patients (for example, those with high attack frequency) may benefit from this treatment.

Allodynia, pericranial muscle tenderness, and imploding and ocular headache may predict the response; BoNT is probably ineffective for the treatment of CTTH.

My clinical experience shows that some headache patients benefit significantly from BoNT treatment. I recommend the combination approach. We need to be able to identify those patients who will best respond to the drug. The results of the pivotal phase III trials are now available as a press release. BoNT was effective for the treatment of chronic migraine.

Full results from the study will soon be available. ■

DR. SILBERSTEIN is a professor of neurology and the director of the Jefferson Headache Center at Thomas Jefferson University, Philadelphia, Penn., U.S.A.

# Large Study Links Early Head Injury and ADHD

*In over 62,000 children studied, medically attended injuries before age 2 were associated with diagnosis.*

BY JONATHAN GARDNER  
*Elsevier Global Medical News*

Children who suffer a head injury requiring medical attention before age 2 are two times more likely to develop attention-deficit/hyperactivity disorder than are children who do not, according to a retrospective cohort study of more than 62,000 British children.

Although the data are interesting, they are not the first to show an association between trauma and ADHD. In an interview with *WORLD NEUROLOGY*, Dr. Robert Findling, who was not affiliated with the study, noted the causal relationship suggested by the data could not be definitely inferred. "It's a 'chicken or the egg' question. Do kids who are impulsive or distractible get head trauma sooner because they're impulsive and distractible?" he asked.

"To presume that head injury is the cause [of ADHD] in a substantial number of people is probably premature," added Dr. Findling, director of child and adolescent psychiatry at University Hospital, Case Medical Center, Cleveland.

The team of American and British researchers, led by Dr. Heather T. Keenan of the department of pediatrics at the University of Utah, Salt Lake City, drew its findings from 62,088 children registered between 1988 and 2003 in the health improvement network, a longitudinal database of primary care practices in the United Kingdom. The database consists of computerized records including information on referrals, diagnoses, treatments, and demographics from 308 practices.

The children were followed from birth until their 10th birthday and were divided into three groups: 2,782 (4.5%) represented those with head injuries, 1,116 (1.8%) had burn injuries, and 58,190 children had neither injury. The investigators considered any child with coding for ADHD, overactive child, attention-deficit disorder, hyperkinetic disorder, or hyperkinetic conduct disorder as having ADHD. Any head injury before age 2 was included except for those coded for minor head injury and nursing advice for head injury.

After adjustment for sex, deprivation, prematurity, and practice, the children who had suffered a head injury before age

2 were 1.9 times as likely as were those who did not to develop ADHD before age 10. Those who suffered a medically attended burn before age 2 had an adjusted risk ratio of developing ADHD of 1.7 before age 10, not significantly different from the head-injury group, the researchers wrote.

However, compared with children who had neither injury, medically attended in-

juries before 2 years of age may be a marker for the subsequent diagnosis of ADHD, the researchers surmised (*BMJ* 2008 Nov. 6 [doi:10.1136/bmj.a1984]).

juries before 2 years of age may be a marker for the subsequent diagnosis of ADHD, the researchers surmised (*BMJ* 2008 Nov. 6 [doi:10.1136/bmj.a1984]).

There did not seem to be a causal relationship between head injury and the disorder, the researchers found. "Some other factor seems to be associated generally with early injury and the development of ADHD," wrote Dr. Keenan and her associates. "We find it plausible that children

who go on to develop clinical ADHD exhibit more risk-taking behaviors as young children, and are therefore more likely to be injured before age 2."

The investigators also found that children with head injuries were slightly younger (median 14 months of age) when injured compared with the burn injury group (median 15 months of age), and the injured children were more likely to be male.

Because of the size of the population studied, the researchers' ability to use a second control group that had experienced early injury, and their ability to follow subjects over time and adjust for known factors related to the development of ADHD, they believe they have been able to make reasonable estimates of the effects of early injury. However, the coding does not clarify the severity of the injuries—a limitation of the study, observed Dr. Findling.

According to Dr. Findling, the estimated prevalence of ADHD is similar in different parts of the world.

"There's this conception that it is a United States-related issue, and in fact, the prevalence seems to be similar [globally]. It's the rate at which it is diagnosed that seems to be different from country to country." ■

**'DO KIDS WHO ARE IMPULSIVE OR DISTRACTIBLE GET HEAD TRAUMA SOONER BECAUSE THEY'RE IMPULSIVE AND DISTRACTIBLE?'**

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## COUNCIL OF DELEGATES MEETING REPORT

## Marrakesh Is the Venue for the 2011 World Congress

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

The 12th Asian Oceanian Congress of Neurology took place at Hotel Ashok, New Delhi, India, Oct. 23-26, together with the 16th Annual Conference of the Indian Academy of Neurology. The meeting boasted many

**BURKINA FASO,  
CAMEROON, AND GUINEA  
WERE WELCOMED  
AS NEW MEMBERS OF THE  
WORLD FEDERATION OF  
NEUROLOGY DURING  
THE COD MEETING.**

participants and was also very well organized. Neurologists from Africa, Europe, North America, and South America, and from the Pan Arab Union of Neurological Societies and the Asian Oceanian Association of Neurology participated. The

former President of India, Dr. A.P.J. Abdul Kalam was the chief guest on the occasion of the inauguration of the conference, and addressed the audience, which added to the status of this important meeting.

The WFN Council of Delegates 2008 was convened at Hotel Ashok Oct. 23 and was well attended.

Prof. Niphon Pongvarin and his team gave an update of the plans for the World Congress of Neurology in Bangkok, Thailand in 2009.

There was a general agreement on the plans for geographical rotation of future world congresses that had been presented at the COD in Brussels back in 2007.

Burkina Faso, Cameroon, and Guinea were welcomed as new members of the World Federation of Neurology.

Prof. Gustavo C. Román (San Antonio) was elected new Trustee after Dr. Marianne de Visser, who has served as Trustee for two periods. Dr. de Visser was thanked for her important contributions to the WFN as the chair of the membership committee.



The WFN trustees pictured left to right are Niphon Pongvarin, Marianne de Visser, Johan A. Aarli, Vladimir Hachinski, Raad Shakir, Ryuji Kaji, and Roger Rosenberg. The delegates convened in India in late October 2008.

As you likely know by now, there were two bids for where the World Congress of Neurology 2011 should be held: Cape Town, in South Africa and Marrakesh, in Morocco. Ultimately, the majority of

the council of delegates voted for Marrakesh.

We delegates all look forward to meeting in Morocco in 3 years. We hope to see you there too! ■

## PROFILES IN NEUROLOGY

## The Practice of Neurology in Morocco

BY MY EL MOSTAFA  
EL ALAOUI FARIS, M.D.

In Morocco, neurology became a specialty distinct from psychiatry in 1975, when the first department of neurology was created at the University of Rabat.

In 1979, the Moroccan Society of Neurological Sciences was created for neurologists, neurosurgeons, and psychiatrists. In 1996, the Moroccan Society of Neurology (MSN) was created, and included all the Moroccan neurologists working in the liberal sector, as well as in provincial and university hospitals. The MSN is member of the World Federation of Neurology, and of the Pan-African, Pan-Arab, and Maghreban neurologic societies, and is an associate member of the European Federation of Neurological Societies (EFNS).

The country currently has just 120 Moroccan neurologists for its 33 million inhabitants. Provincial hospitals in the main cities have at least one neurologist, and there are one or several neurologists in liberal practice who often possess EEG and sometimes EMG appliances.

The MSN organizes two scientific seminars per year, and a national congress every 2 years. The MSN also organizes continuous training courses that focus on the most frequent neurologic diseases (headache, epilepsy, stroke, etc.) for general practitioners in different regions of the country.

At present, 50 neurologists are being trained in the four university departments of neurology; there are plans to train 20-30 neurologists per year by 2010. The training lasts at least 4 years and comprises theoretical lessons and practical

training courses in neurology, including compulsory training courses in clinical neurophysiology, psychiatry, and neuroradiology.

The neurologic pathology in Morocco is characterized by the persistence of certain tropical diseases (such as tuberculo-



Dr. My El Mostafa El Alaoui Faris examines a patient with a chronic neuropathy, with the author's staff in the Hôpital des Spécialités of Rabat.

sis and other infectious diseases) and disorders linked to malnutrition. However, the prevalence of HIV/AIDS remains low, compared with countries in sub-Saharan Africa. On the other hand, changes in diet and the increase in life expectancy have been connected to the emergence of chronic diseases, mainly cerebrovascular diseases (CVD) and neurodegenerative diseases (Alzheimer's disease and Parkinson's disease).

Because of the increased importance of CVD in neurologic practice in Morocco, an epidemiological survey was

started in October 2008 to investigate the prevalence and incidence of the disease and provide CVD prevention and care policy recommendations. The study will continue for 2 years and target 50,000 people.

Several works in clinical neurology

were realized in Morocco, particularly in neurogenetics (discovery of genes involved in ataxias and in Charcot-Marie-Tooth disease), clinical neuropsychology (adaptation of the main neuropsychological tests in Arabic), and infectious and inflammatory diseases (multiple sclerosis and Behçet disease), as well as in epileptology and other areas.

There are 100 computed tomography scanners in Morocco, including those in the main governmental hospitals. There are 30 magnetic resonance imaging scanners, of which 7 are in the university hos-

pitals. Interventional radiology has existed in Morocco for more than 15 years. Endovascular treatment of arteriovenous malformations and arterial aneurysms by specialized neuroradiologists is a common practice. The surgery to relieve symptoms of epilepsy has been practiced since 2005; surgery to lessen symptoms of Parkinson's disease, since 2007. In June, 2008, a Gamma-Knife Perfexion was installed in Rabat, the first unit of this type on the African continent.

Public health insurance had a significant development in 2006, with the implementation of a mandatory medical insurance plan. Currently, 30% of the population has access to this health insurance and it is planned to cover the whole population in the upcoming years.

Moroccan neurology has always been open and welcoming to physicians from across Africa. Morocco organized the Pan-African congress of the neurologic sciences in 1992. Since 2007, African neurosurgeons have been trained in Morocco within the framework of an agreement between the Mohammed V University of Rabat, the Hassan II Foundation of Neurological Sciences, and the World Federation of Neurological Surgery (WFNS). The training includes a 6-month compulsory course in neurology. The MSN and Department of Neurology of the Mohammed V University, with the World Federation of Neurology, suggests setting up a similar training for African neurologists in Rabat. ■

DR. EL ALAOUI FARIS is president of the Moroccan Society of Neurology and professor of neurology at Rabat University, Morocco.

## Disability Worse with Delay

Multiple Sclerosis • from page 1

[comorbidities], 29.4%, mental [comorbidities], and 11.6%, musculoskeletal [comorbidities]," he added.

Visual, autoimmune, and gastrointestinal comorbidities were also reported.

The associated delay between symptom onset and diagnosis was shorter with advancing age at symptom onset. Patients were analysed by age group: younger than 25 years, aged 25-39 years, and aged 40 years and older.

Among the different age groups, the mean time of diagnostic delay was consistently longer if people had vascular, autoimmune, musculoskeletal, or gastrointestinal comorbidities.

However, this effect tended to wane as people aged.

For example, the mean time to diagnosis among those with vascular comorbidities (including diabetes, heart disease, peripheral vascular disease, and hypercholesterolaemia) was almost 9 years longer among those patients under 25 years old, compared with those patients who had no vascular comorbidities in this age group.

But this difference dropped to a mean of 3 years among those aged 25-39 years, and a mean of 1 year among those aged 40 years and over.

The presence of a musculoskeletal comorbidity increased the delay of diagnosis by a mean of 9 years among those patients under age 25 years, a mean of almost 5 years among those aged 25-39 years, and a mean of 2 years among those age 40 years and older.

The association between comorbidity and the degree of disability at the time of diagnosis was also assessed in a subgroup of 2,375 survey participants who were en-

rolled within 2 years of being diagnosed with multiple sclerosis, because their degree of disability would not be expected to change markedly during that period of time.

In that analysis, the risk of having moderate rather than mild disability at diagnosis increased by 51% among those with a vascular comorbidity and by 38% among obese patients.

The likelihood of having severe disability at the time of diagnosis increased by 81% among those patients with a musculoskeletal comorbidity and by 62% among those with a central nervous system comorbidity.

The findings suggest that health care professionals might attribute multiple sclerosis symptoms to a pre-existing condition, which would delay the diagnosis and as a result, increase the degree of dis-

pathophysiologically to increase disease progression," the study's researchers added.

Also during the interview, Dr. Holmøy commented that, in his opinion, the study did have several limitations.

"This is ... a selected group of whites from a volunteer registry, and the numbers are based on self-reports and may differ from other populations," he observed. He was, however, still intrigued by the study's findings.

The study investigators emphasised that the characteristics of the study cohort were indeed similar to the general multiple sclerosis population.

Indeed, two-thirds of the responders were women.

Additionally, the study derived strength from its large size, the authors wrote. ■

**THE LACK OF DIVERSITY IN REGISTRY PARTICIPANTS WAS NOT A STUDY FLAW. MOST WERE WHITE WOMEN, MUCH LIKE THE GENERAL MS POPULATION.**

ability at the time of diagnosis, the authors wrote.

Alternatively, "comorbidities could act

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# Thailand: A Welcoming Land of Contrasts

*The 19th World Congress of Neurology will be held October 24-30, 2009, in Bangkok.*

THE WCN 2009 ORGANIZING COMMITTEE

Thailand is one of the world's most fabled and welcoming countries. The 50th largest country in the world, with a population of 64 million, Thailand has evolved from a rich and implausibly exotic convergence of cultures. Fertile rice plains, towering teak tree-covered mountains, and tropical islands surrounded by powder white sands and fertile seas have attracted Chinese peasants, Burmese invaders, Portuguese explorers, French traders, and waves of Khmer, Mons, Vietnamese, and Malays. All have become subsumed as Thais—an enigmatic, typically fun-loving people who are the backbone of the country formerly known as Siam.

The modern Thai nation sits at the crossroads of Southeast Asia, held halfway between the historic pulls of China and India. However, a more recent layer of influences owes more to Europe, Japan, and Korea. Thailand absorbs it all with a Thai twist.

The Thais are united by a mantra—land, religion, and king. Theravada Buddhism permeates the spirit of the majority of Thai people, instilling a love of peace and tolerance and an uncanny knack for diplomacy. Those skills helped Thailand stay free of colonization despite threats by powers such as Britain, France, and Japan. Apart from land and religion, Thais are passionately united behind King Bhumipol Adulyadej (King Rama IX), the longest-reigning monarch in the world.

In practice, Thai Buddhism has evolved over time to include many beliefs emanating from Hinduism, animism, and ancestor worship. In the southernmost areas of

Thailand, and in some neighborhoods around Bangkok, Islam is prevalent. Several different marginal ethnic groups also populate Thailand, specifically the photogenic hill tribes of Chiang Mai and Chiang Rai. Some of these groups overlap Burma, Laos, Cambodia, and Malaysia, where they have maintained a unique identity despite the imposition of central Thai culture. Historically, China also played an important role in the creation and identity of modern Thai society, especially in the urban commercial sector. A trip to Bangkok is not really complete without enjoying the sights, sounds, and smells of Bangkok's marvelous Chinatown, which the Thais refer to as Yaowarat.

Thailand's up-country life revolves around the fields, the seasons, and the bustling small towns with their morning wet markets. These sit in contrast to the quiet ruined splendor of former capitals and royal cities such as Sukhothai, Lopburi, and Ayutthaya, and the heaving, traffic-choked capital, which has a population of about 9 million.

## Live and Let Live

Proud, united, and peace loving, Thailand is often called the "land of smiles" or the "land of the free." The quest for freedom is epitomized, not so much in the country's political constitution (which is changed often), but in a live-and-let-live culture of tolerance and noninterference. Individual expression is matched by a passion for national unity, especially in times of crisis. This was very apparent after the highly destructive financial storm of 1997 and 1998, when Thais rallied to buy Thai products and affirm national unity in defiance of global economics.

Bangkok is 50 times the size of the coun-



MARK HALLETT

**No visit to Bangkok would be complete without visiting the dazzlingly beautiful Grand Palace, the city's most famous landmark. It is indeed a must-see.**

try's second city (Chiang Mai); its name translates poetically as "village among the plum olive trees." More formally, the megapolis has a much longer, more imposing celestial name in court Thai. It is "Great City of Angels, the Supreme Repository of Divine Jewels, the Great Land Unconquerable, the Grand and Prominent Realm, the Royal and Delightful Capital City Full of Nine Noble Gems, the Highest Royal Dwelling and Grand Palace, the Divine Shelter and Living Place of the Reincarnated Spirits." On a visit to impressive Grand Palace and Temple of the Emerald Buddha, the name seems appropriate.

Contradiction and contrast are at the center of Bangkok life: the bejeweled high society dame stopping her BMW to buy noodles from a street vendor; the elegant skyscrapers sitting side by side with wooden shacks full of migrant laborers; ochre-robed monks receiving rice from iPod-carrying early morning commuters who remove their shoes to donate alms in exchange for a spiritual blessing.

Modern Bangkok dominates all social, political, economic, educational, religious, and commercial aspects of modern Thailand. With its strategic geographic location in Asia, it is not surprising that the Thai capital is serviced by over 70 airlines from around the world. But the real Bangkok can often be better enjoyed by trying more exhilarating local versions of transport. No one has truly arrived there until they've taken a hair-raising three-wheeled tuk-tuk taxi ride, or ridden on the Chao Phaya river of kings on a long-tail boat taxi. A totally new perspective on Thai life opens on the river. For all its modernity, the most memorable images of Bangkok are often the timeless scenes of old and young Bangkok residents going about their lives in wooden houses along the Chao Phaya and its adjacent canals.

Again it is often the implausible contradictions and the contrast of old and new, rich and poor, ugly and beautiful, the spiritual and physical living side by side that epitomizes Thai culture, at least to foreign eyes. A visitor is never far away from marvelous elements of this cultural heritage. Even the whirlwind view of Thai culture offered by floating markets, masked dancers, souvenir shops, cabaret shows,

kick boxing stadiums, and riverside restaurants never fails to evoke a rich civilization that excels at embracing new influences and adapting to them.

## A Question of Taste

Nowhere is the triumphant Thai melting pot of cultures more celebrated than at the dining table. Spicy—and often not spicy—Thai cuisine is a kaleidoscope of ingenious, beguiling, and surprising tastes, aromas, textures, and visual innovation. Wonderful Thai dining moments occur in streetside stalls, at beachside seafood restaurants, on picnic mats in up-country sojourns, and at some of the most chic dining establishments in Asia. Whether your fancy is the Muslim- and Malay-influenced curries of the south, the seafood platters of the Andaman, the Vietnamese and Isan vegetable dips and dishes from northeast Thailand, or the visually ornate and subtle contrasts of royal Thai cuisine from Ayutthaya and Bangkok, a trip to Thailand is no time to start a diet. Unquestionably, cuisine is Thailand's greatest gift to the world.

## The Reviews Are In

The modern face of Bangkok has rapidly changed in the past 10 years. Skyscraper construction, which halted during the 1998 economic meltdown, is in full swing again. Many of the new developments have followed the route map of the Bangkok Mass Transit System (BTS) Skytrain rail network that opened in Bangkok in 1999. The clean, reliable, and efficient skytrain and Mass Rapid Transit Authority (MRT) underground networks have improved life in the capital for hundreds of thousands of commuters, students, and visitors alike.

In 2008, the readers of *Travel + Leisure* magazine voted Bangkok the World's Best City 2008 (the other top four were Buenos Aires, Cape Town, Sydney, and Florence). Scoring was evaluated on five criteria: sights, culture and arts, restaurants and food, people, and value. In the Best Asian City category, Kyoto came 2nd after Bangkok; Chiang Mai was third.

So that's the proof. On your next trip, make sure you leave enough time to explore one of the great destinations of the world. The people of Thailand are ready to welcome you. ■

## After Bangkok, We'll Meet You in Marrakesh in 2011!



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**After next year's Congress, to be held in Bangkok, the 2011 World Congress of Neurology will be held in Marrakesh, Morocco. The WFN's Council of Delegates voted on the site at their recent meeting (reported in greater detail by President Aarli on page 6), choosing Marrakesh—city of the famed Seven Saints, at the foothills of the Atlas Mountain. The other candidate was Cape Town, South Africa. Congratulations to both cities. We look forward to seeing you in Morocco in 2011!**

# Gene Therapy for Prion Disease?

BY JEFF EVANS  
AND DENISE NAPOLI  
*Elsevier Global Medical News*

**T**herapeutically blocking the expression of prion protein in mice that have begun exhibiting symptoms of prion disease extends their survival and delays symptoms, according to gene therapy research that uses RNA interference.

The study is the first to use RNA interference (RNAi) therapeutically in vivo in prion disease through a single hippocampal injection of lentivirally mediated RNAi, which produces a short hairpin RNA molecule that blocks the expression of cellular prion protein (PrP).

Other experiments have shown that transgenic mice produced by lentiviral transduction of embryos have an increased resistance to prion infection because of their expression of anti-PrP short hairpin RNA molecules.

“Our findings further support therapeutic strategies directed at PrP knock-

inoculation because mice thereafter became clinically sick and some of the mice treated with RNAi showed early scrapie symptoms (*Proc. Natl. Acad. Sci. U.S.A.* 2008;105:10238-43).

Treatment with just one focal dose of RNAi significantly prolonged mean survival in the mice (105 days, range of 87-129 days), compared with receipt of an empty lentivirus (88 days) or no virus (85 days).

This amount of increased survival “was strikingly large with respect to the very small volume of brain targeted,” which “may result from direct or indirect effects of localized neuroprotection or may simply be due to the reduction of

PrP expression at a critical, or rate-limiting, site for prion replication,” they wrote.

This treatment protected against hippocampal neuronal loss and was associated with reduced levels of spongiosis and pathogenic PrP accumulation in the hippocampus.

In evaluations of whole-brain pathology, mice treated with RNAi also showed a reduction in spongiosis and pathogenic PrP deposition in the thalamus and cortex, which “likely reflects altered prion spread and replication in these areas after hippocampal PrP knock-down by lentiviral injection, rather than more widespread PrP de-

pletion arising from spread of virus,” the investigators wrote.

Dr. Mallucci, who is the program leader of the MRC Toxicology Unit at the University of Leicester (England), as well as a consultant neurologist at the Dementia Research Center in London, added that RNA interference therapy has successfully been applied in areas outside of prion disease, including in mouse models of ALS, Alzheimer’s disease, Huntington’s disease, and a model of SCA1. Other gene therapies for prion disease currently being investigated include dominant negative prion protein delivered by lentivirus to inhibit prion replication, she added. ■

**‘THE PROBLEM OF EARLY DETECTION OF DISEASE IN PATIENTS IS STILL A HUGE STUMBLING BLOCK’ BEFORE FUTURE THERAPIES CAN OCCUR.**

down for the treatment of prion diseases and are also relevant for neurodegeneration more widely, highlighting the importance of intervention when neuronal dysfunction can still be reversed,” wrote Melanie D. White, Ph.D., and her coinvestigators. Dr. White conducted the research with her associates at University College London, but she is now at the University of Edinburgh. “The approach used here paves the way not only for possible future therapy but also for mechanistic dissection of toxicity and recovery in prion diseases.”

Although the results are indeed promising, in an interview with *WORLD NEUROLOGY*, Prof. Giovanna Mallucci, another researcher on the study, said: “The problem of early detection of disease in patients is still a huge stumbling block. Treatment must be given early before brain cells are dying, ideally.” Another issue is the blood-brain barrier, which makes drug delivery a real problem, just as it is for other neurodegenerative diseases, she added.

In mice that had been intracerebrally inoculated with prions at age 1 week, treatment with lentivirally-mediated RNAi at 8 weeks preserved burrowing-activity and object-recognition memory between 9 and 11 weeks post inoculation, unlike infected mice that received an “empty” lentivirus or no virus at all.

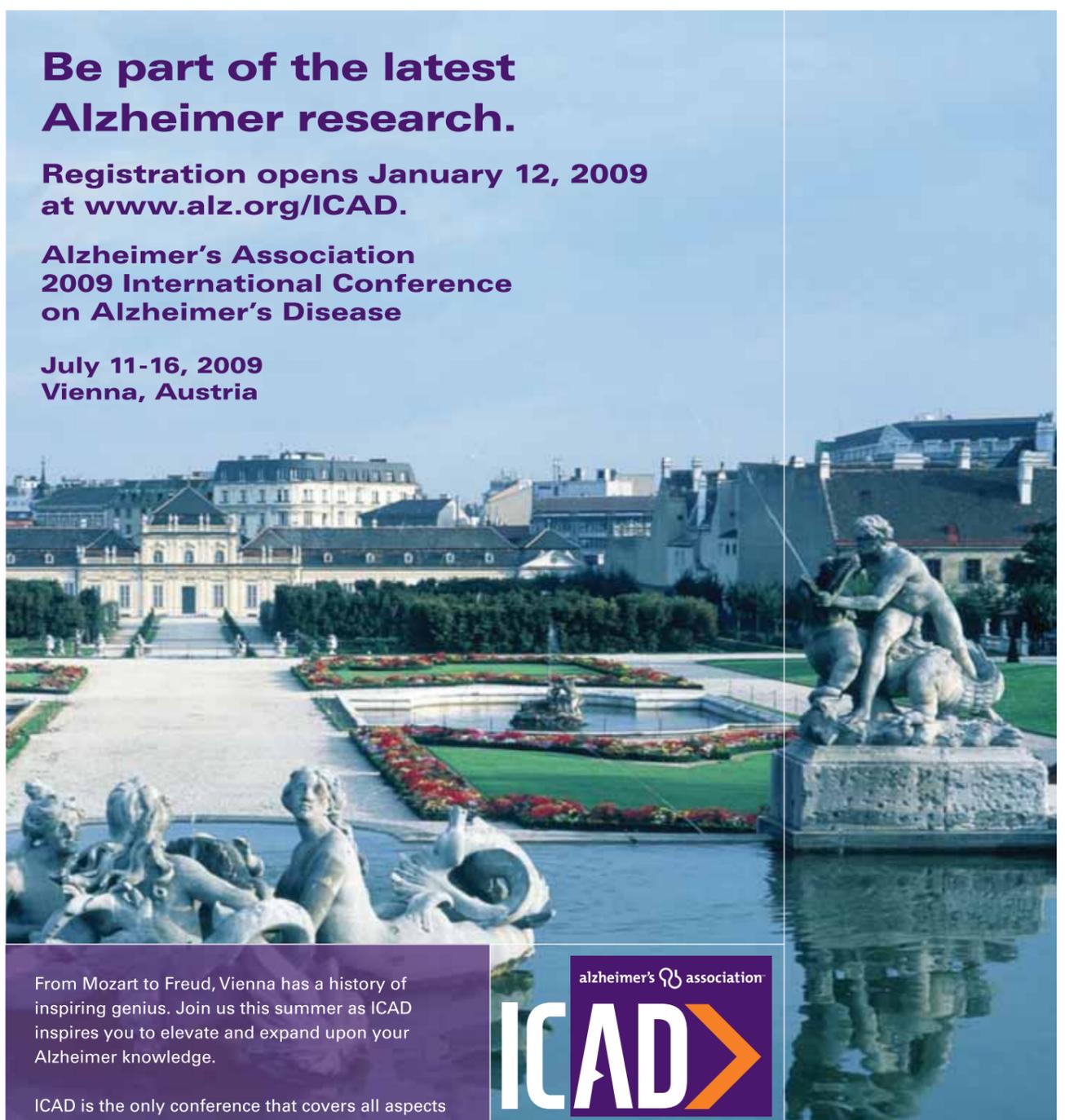
The latter mice experienced significant declines in these behaviors, which are hippocampal-dependent tasks. Observations were not extended beyond 11 weeks post

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EPDA president Stephen Pickard speaks to the media at the launch in Madrid.

## EPDA Calls for New Drug Therapies, Less Bureaucracy

In Madrid on Aug. 25, alongside the European Federation of Neurological Societies congress, the European Parkinson's Disease Association (EPDA) launched its pan-European Parkinson's Awareness Campaign and Kit, called: "Still Life With Parkinson's—Parkinson's Is Visible—Make It Livable."

The campaign, which is aimed at decision makers, scientists, health care professionals, people with Parkinson's, their families, and the general public, is ongoing and will continue to raise awareness about the impact that Parkinson's has on daily life by improving the understanding and knowl-

edge relevant for all disease stages.

An estimated 1.2 million people in Europe have Parkinson's, and this number is increasing as the demographics continue to change.

EPDA President Stephen Pickard said, "Parkinson's is a costly disease and places a huge burden on careers and society as a whole. We need governments to realise that taking action to reduce this burden by ensuring people receive the best care and treatment available makes the most economic and social sense."

Dr. Fabrizio Stocchi, a member of the EPDA's medical advisory board, called on the pharmaceutical companies to develop new medicines to slow the progression of the illness and come up with treatments with fewer side effects.

He also urged the European Union to overhaul regulatory procedures for existing drugs.

"There is a crucial need for better treatments with fewer side effects and simpler methods to administer drugs as some patients have to take their medications five, six, or even seven times a day," he said.

"Over the past 20 years, there has been a great improvement in treatment, but drug companies still must spend more on research."

Additionally, Mr. Pickard called for a European Union-wide reimbursement policy.

"In theory, the European Union is a harmonized market and the pharma sector should be also, but seven countries decide their reimbursement policies individually and medicines are not evenly available," he pointed out.

"Pharma companies launch their products in the biggest markets first, so while patients in Germany have access to a new drug, those in nearby Lithuania have to wait several years," he said.

"We need the decision makers to take Parkinson's more seriously, for example, by reimbursing drug costs at higher levels and removing restrictions on expensive treatments."

The campaign has the support of many organizations, including the World Health Organization's Working Group on Parkinson's Disease, the World Federation of Neurology, the European Federation of Neurological Associations, the European Federation of Neurological Societies, the National Tremor Foundation (UK), the pharmaceutical industry, and patient organizations located all around Europe.

In 2009, the EPDA is planning to hold a media roundtable meeting, lobby the European Parliament, and develop a lobbying tool that will help the 41 EPDA member organizations to use the translated Awareness Kit effectively in their countries to raise awareness and effect change.

Awareness Kits are available free of cost by contacting [info@epda.eu.com](mailto:info@epda.eu.com).

Further information can be found by visiting the EPDA's Web site, online at [www.parkinsonsawareness.eu.com](http://www.parkinsonsawareness.eu.com). ■

A report from the European Parkinson's Disease Association.

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THE LEADER IN NEWS AND MEETING COVERAGE

# Calendar of International Events

## 2009

**37th Annual International Neuropsychological Society Meeting**  
February 11 - 14, 2009  
Atlanta  
[www.the-ins.org/meetings](http://www.the-ins.org/meetings)

**2nd Asian and Oceanian Parkinson Disease and Movement Disorder Congress**  
February 15 - 17, 2009  
New Delhi  
[www.aopmcindia.com](http://www.aopmcindia.com)  
**5th Annual Update Symposium Series On Clinical Neurology & Neurophysiology**  
February 16 - 17, 2009  
Tel Aviv  
[www.neurophysiology-symposium.com](http://www.neurophysiology-symposium.com)

**2nd European Brain Policy Forum**  
February 25 - 26, 2009  
Brussels  
[www.kenes.com/ebpf2009](http://www.kenes.com/ebpf2009)

**9th International Conference on Alzheimer's and Parkinson's Diseases: Advances, Concepts and New Challenges**  
March 11 - 15, 2009  
Prague  
[www.kenes.com/adpd](http://www.kenes.com/adpd)

**5th World Congress of the World Institute of Pain**  
March 13 - 16, 2009  
New York  
[www.kenes.com/wip](http://www.kenes.com/wip)

**4th Fred J. Epstein International Symposium on New Horizons in Pediatric Neurology, Neurosurgery and Neurofibromatosis**  
March 15 - 19, 2009  
Eilat, Israel  
[www.fredhorizons.com](http://www.fredhorizons.com)

**24th Conference of Alzheimer's Disease International**  
March 26 - 28, 2009  
Singapore  
[www.adi2009.org](http://www.adi2009.org)

**2nd International Symposium on Psychogenic Movement Disorders and Related Conversion Disorders**  
April 2 - 4, 2009  
Washington  
[www.movementdisorders.org/education/pmd](http://www.movementdisorders.org/education/pmd)

**The Innsbruck Colloquium on Status Epilepticus 2009**  
April 2 - 4, 2009  
Innsbruck, Austria  
[www.innsbruck-SE2009.eu](http://www.innsbruck-SE2009.eu)

**61st Annual Meeting of the American Academy of Neurology**  
April 25 - May 02, 2009  
Seattle  
[www.aan.com](http://www.aan.com)

**6th Baltic Congress of Neurology (BALCONE)**  
May 13 - 16, 2009  
Vilnius, Lithuania  
[www.balcone2009.com](http://www.balcone2009.com)

**1st International Course on Pain Medicine**  
May 28 - 31, 2009  
Granada, Spain  
[www.icpm.net](http://www.icpm.net)

**15th Annual Meeting of the Organization for Human Brain Mapping**  
June 18 - 22, 2009  
San Francisco  
[www.humanbrainmapping.org/sanfrancisco2009](http://www.humanbrainmapping.org/sanfrancisco2009)

**Association of British Neurologists Annual Meeting**  
June 22 - 26, 2009  
Liverpool, England  
<http://abn.org.uk/meetings/>

## 2010

**36th Annual Meeting of the North American Neuro-Ophthalmology Society (Nanos)**  
March 6 - 12, 2010  
Tucson, Ariz., U.S.A.  
[www.nanosweb.org/meetings](http://www.nanosweb.org/meetings)

**10th Eilat Conference on New Antiepileptic Drugs**  
April 25 - 29, 2010  
Eilat, Israel  
[www.eilat-aeds.com](http://www.eilat-aeds.com)

**International Child Neurology Congress: ICNC 2010**  
May 2 - 7, 2010  
Cairo, Egypt  
[www.icnc2010.com](http://www.icnc2010.com)



Welcome to the

# 19<sup>th</sup> World Congress of Neurology

24–30 October 2009 • Bangkok, Thailand



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in Neurology

Deadline for abstract submission is 29 April 2009. For more information regarding abstract submission and guidelines, visit [www.wcn2009bangkok.com](http://www.wcn2009bangkok.com)



Dr. A.P.J. Abdul Kalam, former president (People's President) of India, inaugurated the conference.

## 1,085 Delegates Attended

AOCN-IANCON • from page 1

► Dr. Vladimir Hachinski gave the J.S. Chopra Oration: Should Everyone Do Research?

Just as there is every year, there was a well-attended and appreciated session on multiple choice questions for the post graduates and the consultants. Three awards were given for the best score in the multiple choice questions. Four symposia were delivered on cerebrovascular disorders, pain management, stem cell transplantation research and therapeutics, and HIV/Neuro AIDS. All were uniformly excellent.

The clinicopathological session generated a lot of interest. It focused on the autopsy of a young HIV-positive boy with measles inclusion body encephalitis (MIBE).

The pathologist who presented the case did an excellent job of showing how the findings from clinical studies done at autopsy supported the diagnosis.

Three breakfast seminars were held, on behavioral neurology, neuromuscular disorders, and dementia. Each session was well attended by

more than 100 delegates, and all generated productive discussions.

The conferences ended on a note of agreement that activities had gone on smoothly and were discharged in a timely fashion.

Because this conference was specifically planned and organized to occur just before Diwali (the Festival of Lights), all of the delegates enjoyed the sociocultural activities as well. ■

DR. MEHNDIRATTA was the organizing secretary of AOCN-IANCON 2008.

He is also a professor of neurology at G.B. Pant Hospital, New Delhi, India.

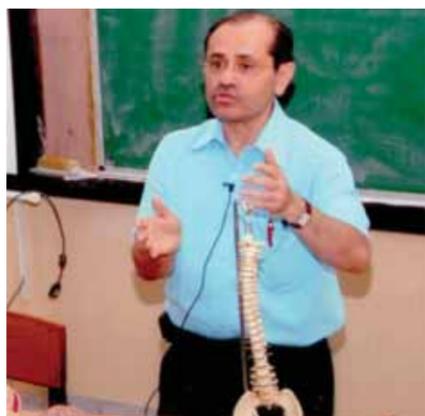
## Entrepreneurs: Teaching Neurology to Primary Care Physicians

BY APOORVA PAURANIK, M.D.

I belong to a small group of neurologists in developing countries who teach neurology to MBBS and MD (internal medicine) students in small medical colleges that lack independent departments of neurology or residency training programs.

The abysmally low ratio of only one neurologist per one million population in India is not going to improve anytime soon. On the other hand, thousands of students are seeking an MBBS in primary care and hundreds are pursuing an MD in internal medicine. Primary care physicians and internists are going to provide neurology services to a far larger proportion of the population in small towns and villages rather than doctor of medicine (DM) neurology degree holders for the foreseeable future.

Hence it is crucial and important that the neurology component of this basic



Dr. Pauranik's plans include a neurology Web site in Hindi for the general public.

level of medical education is up to date and meets high standards, with a faculty of trained and committed neurologists rather than internists.

My love of teaching combined with fluency in both English and Hindi have been the foundation of my advocacy and leadership skills. I have received many international awards, including the Parke Davis International Award for Epilepsy Services (1993); membership in the Public Education Commission of the International Bureau for Epilepsy (IBE) (1993-1997); a grant from the International League Against Epilepsy for public education (1994-1995); a grant from the Rotary International Foundation (Evanston, Ill.) for upgrading an epilepsy clinic at M.Y. Hospital, Indore,

India; and graduation from and mentorship in the Donald M. Palatucci Leadership Forum of American Academy of Neurology on advocacy.

I am the publisher, author, and editor of Neuro-Gyan, a 20-page monthly magazine in Hindi. Each issue is dedicated to a specific neurologic disease and mailed, free of cost, to patients with the relevant disease. I have authored and published first-time textbooks on epilepsy, Parkinsonism, cerebral palsy, and many more.

I have produced educational programs on epilepsy and aphasia, among other conditions, which have been repeatedly broadcast on national television.

I have been dedicated to initiating and sustaining self-help groups for people with a variety of neurologic diseases. I have played the role of catalyst with respect to many diseases such as epilepsy, spinal cord injury, paraplegia, multiple sclerosis, and dyslexia. I have organized many health camps and health fairs.

I have organized an interstate Neuro-Quiz competition for medical students including undergraduates, interns, and postgraduates with the aim of increasing the awareness and popularity of neurology and to encourage a competitive spirit. The first round of the quiz comprising 100 multiple choice questions is held simultaneously in 30 medical colleges in six Indian states. All participants carry home the question and answer book explaining the reasons and facts about correct choices along with references. They also receive a set of interesting and colorful bookmarks depicting neurology-related graphics and quotations as a token of appreciation and also as souvenirs.

Each year I organize the Madhya Pradesh state-level Annual Neurology Certificate Course for internists and family physicians at Indore. The course takes place during last week of November and each year 100 MDs join in. The majority of them are from remote rural districts, serving in government-run primary care health centers. Others are private practitioners and general duty medical officers working in medium-sized private hospitals. The syllabus covers basic and practical aspects of clinical neurology relevant to primary care settings with limited sources. All trainees are given a neurology examination kit; aprons; handouts of lectures; and a disc contain-



Dr. Apoorva Pauranik teaches neurology to medical students who plan to go into internal medicine and primary care.

ing text, images, and videos. The whole exercise is an excellent example of private-public partnership.

I have compiled, edited, and published a neurology pocket guide for residents in internal medicine for free distribution in medical colleges

My research interests are aphasia, dyslexia, and neurolinguistics. Not much work has been done in Indian languages in this field. I have been working to develop diagnostic and therapeutic resources for assessment and rehabilitation of Hindi monolingual and Hindi-English bilingual patients with aphasia and related disorders.

My home state of Madhya Pradesh is one of last few large ones in India with no independent departments of neurology (or neurosurgery) in government medical colleges. I lobbied hard to convene a meeting at the Directorate of Medical Education at Bhopal in August 2005, which was attended by representatives from five medical colleges. The principal secretary in the ministry of medical education presided over the meeting. Dr. M. Gourie Devi, past president Neurological Society of India, was invited as the guest expert. I was entrusted to make a plan of various requirements of staff, equipment, and other budget items, which I did meticulously. Unfortunately, the proposal(s) have not moved forward despite my follow-up. Instability and changes in political and administrative posts resulted in loss of crucial support at higher levels. I hope this profile in WORLD NEUROLOGY and subsequent letters from its officeholders to concerned authorities in Madhya Pradesh will spur the process again.

Discussion about education need not eclipse the fact that my primary occupation is caring for patients with neurologic diseases. I see patients in a public hospital outpatient division, in my private office, and in wards for about 12 hours a day. My dreams are to:

► Launch and sustain a long-term, high-intensity, wide-spread program for public and patient education in Hindi through publication and saturation-level dissemination of a large variety of pamphlets, brochures, posters, booklets, books, and electronic multimedia resources dedicated to various aspects of each neurologic element.

► Launch, develop, expand, and maintain a comprehensive Web site in Hindi dedicated to neurology education for the general public and patients. Literacy rates and educational levels have improved in India, resulting in a demand for medical information. But science journalism, including medical science, has not come of age in Indian languages. Despite being the fourth most commonly spoken language in the world, Web sites in Hindi are hard to find on the Internet. But this will change soon. Within the next few years broadband access to the Internet will reach the vast rural hinterland of India where not more than 1%-2% of the population understands English. The proposed Web site, along with its print version of monthly magazine will usher a new era of cooperation, sharing, advocacy, activism, and group action by individuals concerned about different neurologic diseases.

► Establish a national-level network of patient support groups for common as well as rare (orphan) neurologic diseases in an ever-expanding number of cities in India with additional periodic joint meetings of these groups (neurologic sangam). ■

DR. PAURANIK is a consultant neurologist and assistant professor of medicine at M.G.M. Medical College and M.Y. Hospital, in Indore, India.

# Advocacy: Become a Five-Star Neurologist

*The best physicians do more than just diagnose.*

BY MICHAEL FINKEL, M.D. AND  
M.M. MEHNDIRATTA, M.D.

Despite the tremendous growth of the scientific knowledge and capabilities of modern neurologic medicine, it has become apparent to many leading practitioners that science, technology, and pharmacology are useful only if they can be applied to the needs of neurologic patients and families. All societies face situations where all levels of care, from basic to sophisticated, are limited by regulations, restrictions, and funding. At the first International Teaching Course in Neurology, held in Dakar, Senegal, in June 2008, Amadou Diop Gallo challenged each participant to become a “five-star” neurologist and accept the simultaneous roles of caregiver, researcher, trainer, manager, and communicator. These are not innate abilities; they are skills that are taught, learned, and refined.

Because of the pioneering efforts of the late Dr. Donald Palatucci and the late Dr. Kenneth M. Viste Jr., the American Academy of Neurology acted. Drawing upon the U.S. social tradition of citizen involvement, the AAN developed a program to train neurologists to advocate effectively for our patients, their families, and our specialty.

The Palatucci Advocacy Leadership Forum (PALF) has become an amazingly successful training program, training 30 neurologists per year in the skills needed for effective advocacy.

Three members of each PALF class are international neurologists, and PALF graduates from India, Pakistan, Sri Lanka, and the Philippines wanted to teach these principles to their colleagues in their home countries.

The Asian Oceanian Association of Neurology and Indian Academy of Neurology provided the venue for this new area of neurologic education when they held their first advocacy workshop during the combined 2008 Congress. AOAN and IAN members invited former PALF graduates to participate in this session, which was open to all congress attendees at no charge.

Since the usual PALF sessions take place over several days, we PALF graduates worked with AAN staff members Melissa Larson and Amy Kaloides to design a program to introduce the principles of advocacy in the 6 hours allotted to the workshop.

The program explained why advocacy is part of the job of every neurologist, and then taught the participants how to formulate their ideas clearly and to present them effectively to government ministers, elected officials, and reporters from several types of media.

PALF graduates presented their Action Plans and explained how they were developed and implemented. Video examples from PALF training sessions were used to exemplify what to do and what to avoid. Every attendee then developed an action plan that was critiqued by the group, and then underwent a mock media interview that was surgically dissected by the rest of the audience.

The results of this rigorous analysis were quickly seen, as participants learned from each other and from the opportunity to present a second time. The mentors were gratified by the speed with which attendees were able to adapt during this short period. The session finished with each participant completing a critiqued action plan that was ready to put into action upon their return to their home countries.

The success of the workshop impressed the WFN Trustees who attended, and the Trustees decided to add a session on advocacy at the 2009 World Congress of Neurology in Bangkok. All attendees are encouraged to put this important workshop on their “must attend” list for Bangkok. The Indian PALF graduates have founded a Section of Advocacy in the Indian Academy of Neurology, and this workshop will give attendees the skills needed to do the same in our WFN societies worldwide. ■

DR. FINKEL is a neurologist in private practice in Naples, Fla., U.S.A. DR. MEHNDIRATTA is a professor of neurology at G.B.Pant Hospital, New Delhi, India.



Pictured are, back row, left to right: Lakshmi Ranganathan, M.D., India; Tarakad Ramachandran, M.D., U.S.A.; Michael Finkel, M.D., U.S.A.; Melissa Larson, AAN staff; front row: Amy Kaloides, AAN staff; Mohammad Wasay, M.D., Pakistan; Apoorva Pauranik, M.D., India; M.M. Mehndiratta, M.D., India.

## PROFILES IN NEUROLOGY

## The Practice of Neurology in Uruguay

The neurology community in Uruguay consists of a relatively small team of colleagues (around 100 adult neurologists) who share a common training path and postgraduate education experience. All of us know each other, we enjoy team-work and are always enthusiastic about activities that involve regional or international exchanges and further training. However, as is the case in most developing countries, we face many difficulties.

Here in Uruguay, we have a single Public School of Medicine, which houses the only Neurological Institute in our country. Founded in 1926, the Neurological Institute includes an adult neurology department, a child neurology department, and a neurosurgery department.

This is where all neurologists in my country receive our 4 years of specialty training in neurology. In recent years, an additional postgraduate education program, intended for certified neurologists, has been developed with the support of the WFN.

Our current health system promotes part-time positions, while providing relatively low salaries. Consequently, most of us are involved in some combination of work in both public and private hospitals, and/or work in several private institutions.

On the public side, the Neurological Institute resides mainly in the University Hospital, the Hospital de Clínicas. The adult neurology branch includes clinical neurology, as well as neurophysiology and neuropsychology. The staff consists of the director, permanent staff associate professors, assistant professors (a position that has a 3- to 6-year duration), neurology assistants (3-year duration), and

residents/trainees. With the exception of residents, all other staff members dedicate a standard part-time work schedule (12-24 hours per week), usually during the morning hours. For example, I have been an assistant professor since 2007. As such, my tasks on weekday mornings include: daily supervision of our neurology outpatient clinic, bedside teaching, consultations for patients admitted to the internal medicine department, and participation in our daily academic meetings, such as rounds and conferences.



BY PATRICIA BRAGA, M.D.

Private practice commonly includes general neurology outpatient clinics for patients over age 15, along with some days of on-call neurology covering the ER and inpatient services. In each institution

some neurologists are responsible for nonurgent, specialist consultations on patients already admitted, while others provide in-house consultations for chronic patients, who are unable to attend the hospital's standard outpatient clinics for follow-up.

Despite the complex health care system, colleagues in most public and private institutions are able to organize meetings once or twice a month to discuss challenging patients, and update the group on professional topics of interest.

We have no boards here in Uruguay for subspecialization in neurology—yet. However, since the 1960s, different academic sections have been established within the Neurological Institute. In these sections we exchange clinical experience, teach residents and younger neurologists, and perform clinical research.

Research is encouraged, but not included in our daily scheduled duties; therefore, it can only be performed during our

free time. Moreover, no funding is usually available for clinical research.

In my experience, the most frequent symptoms and neurologic diseases found in the outpatient setting are headache, vertigo, and epilepsy in the younger population; and dementia, Parkinson's disease, and polyneuropathies in the older patient group. In the ER, consultations are usually requested for patients presenting with acute stroke, trauma, status epilepticus or seizure clusters, and other causes of impaired consciousness.

Since most hospitals in Uruguay do not have a separate neurology unit, patients with neurologic diseases are usually admitted and managed by internists. It is up to them to determine if there is a need to also involve the neurologist in the patient's care. In this setting, the most common diseases referred for neurologic consultation include stroke, neurologic complications of infectious illnesses (such as AIDS), neurologic symptoms in the context of autoimmune or systemic oncologic diseases, and postsurgical neurologic complications. Other frequent consultations are requested for the management of chronic disorders such as epilepsy, Parkinson's disease, or myasthenia in patients admitted for unrelated medical or surgical co-morbidities.

All specialized treatments available at the university hospital are offered free to the users of the university or public health system. These treatments are also offered to private patients for a low institutional fee. In this context, an epilepsy surgery program has been working since 1999, performing mainly temporal resection surgeries, some extratemporal cases, and a few disconnection procedures. Invasive treatments for Parkinson's disease are also being developed, including ablation and neurostimulation procedures, when patients can afford the cost of the device.

Concerning diagnostic tools, standard

neurophysiologic and neuroradiologic procedures are commonly performed, although access to MRI can be limited because of financial constraints. Of course, our training has placed a lot of emphasis on developing our clinical diagnostic skills, which in turn help us to optimize allocation of resources. Serologic studies for prevalent infectious diseases are usually available. In addition, genetic and molecular tools have been developed for a number of diseases (such as fragile X syndrome, and some of the dystrophies), but in many cases the collected specimens have to be sent abroad.

There are times when we cannot avoid a feeling of frustration, thinking that things would have been much easier if only additional tests were available or if appropriate studies could be done in a more timely manner. Another frustration is that access to most drugs is delayed, compared with access in developed countries. Therefore, there is often a treatment gap between our public and private system users, especially when a new medication first appears. Not infrequently, we are unable to secure continuous availability of certain drugs, particularly for patients who are under the care of our public or university hospitals. For these reasons, we are used to devoting time during our daily practice to perform an individualized evaluation of our patients' financial means and risks of noncompliance before selecting medication. Frequently, we also must give practical recommendations on how to obtain the prescribed medication.

Cost, drug availability, and training in Uruguay are challenges. Although the international community is generous, we neurologists know we must be the main promoters of progress. ■

DR. BRAGA is an assistant professor of neurology at the Institute of Neurology in Montevideo, Uruguay.

## Junior Traveling Fellowship Report: International Symposium on TAST

Thanks to the WFN, I attended the 10th international symposium on Thrombolysis and Acute Stroke Therapy (TAST), in Budapest Sept. 21-23. It was on one of the most important topics in neurology: the acute treatment of stroke with a focus on thrombolysis and other measures to improve reperfusion. I am a resident in neurology here in Ethiopia, and this meeting gave me an insight into the latest approaches in the management of patients with stroke.

For me, the majority of the papers presented by different experts in the area of stroke were

very interesting and new. The practice in the developed world is quite different from what we do here, where the management of stroke involves no more than just attending to basic life support measures, treatment of other associated conditions like hypertension, prevention of complications of the paralysis, and rehabilitation for the survivors. In fact, these are also important measures to be taken, though the facilities differ. Thrombolysis is unthinkable in our setup because we lack both the trained medical personnel and the necessary facilities.



BY BELACHEW D. ARASHO, M.D.

Stroke is currently increasing as one of the major reasons for hospital admissions in the developing world, causing an enormous economic burden. In response to this crisis, we have to increase our level of care for

stroke patients. Attending meetings such as TAST with experts in this field could be one of the steps in our effort to build our capacity to this effect. In addition to the scientific discussions, these kinds of in-

ternational seminars will give us a chance to know people from all over the world. ■

DR. ARASHO is a neurology resident at Addis Ababa University, Ethiopia.

## Deadline for Junior Traveling Fellowships

The WFN is able to offer twice the number of Junior Traveling Fellowships in 2009. Candidates for traveling fellowships are young neurologists from countries classified by the World Bank as low or lower middle income. The fellowship is to travel to an approved international meeting.

There will be 20 awards. Applicants may be no older than

42 years and should not hold a post above associate professor. They should send the name and dates of the meeting they wish to attend, their CV and bibliography and a letter of recommendation from their department head. If they have been selected to present a paper or poster, their application should include an abstract. The application also should in-

clude an estimate of expenses, not over £1,000.

Applications may be sent to [info@wfneurology.org](mailto:info@wfneurology.org) or to World Federation of Neurology, Hill House, Heron Square, Richmond, Surrey, TW9 1EP, United Kingdom, and must be received by Feb. 20, 2009. Awards will be announced by the end of March.

# Leading resources in clinical neurology!

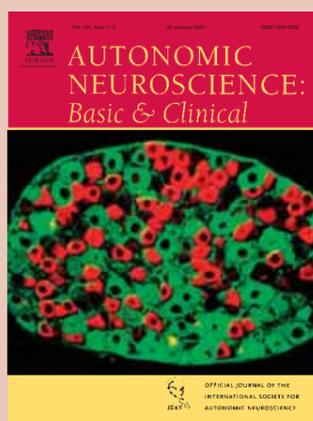
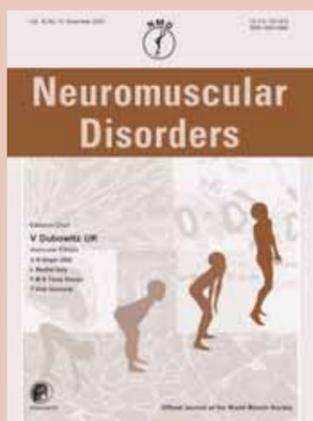
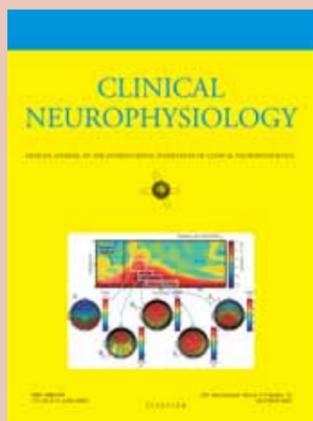
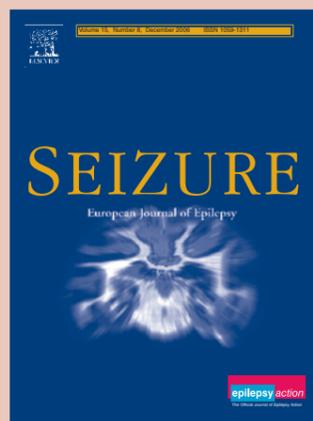
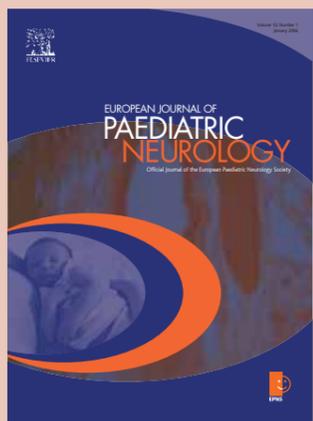
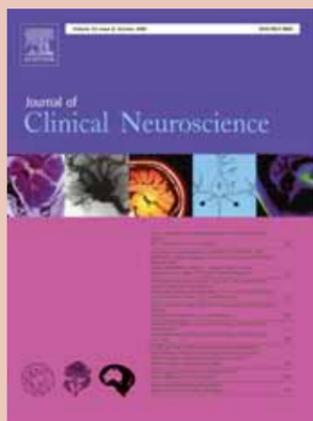


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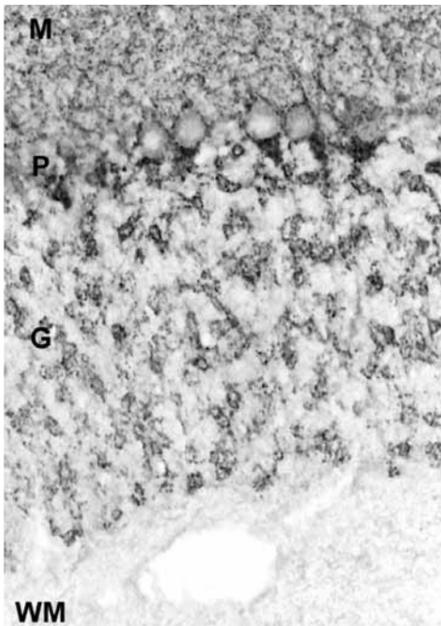
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# GAD Antibodies Linked Not Just to Stiff Person Syndrome

BY ALBERT SAIZ, M.D.,  
AND FRANCESC  
GRAUS, M.D.

**A**ntibodies to glutamic acid decarboxylase, the rate-limiting enzyme for the synthesis of the inhibitory neurotransmitter  $\gamma$ -aminobutyric acid, were initially recognized in the serum and cerebral spinal fluid of patients with stiff person syndrome, a rare central nervous system disorder characterized by progressive muscular rigidity, predominantly of the trunk muscles, with superimposed spasms.

The syndrome is frequently associated with other autoimmune diseases, mainly type 1 diabetes. Indeed, antibodies to glutamic acid decarboxylase (GAD) were seen in about 80% of newly diagnosed diabetes patients.



Rat cerebellar section with GAD-ab serum shows robust GAD immunoreactivity—M: molecular layer; P: Purkinje layer; G: granular; WM: white matter.

GAD antibodies have since been reported in a subgroup of patients with late-onset isolated cerebellar ataxia (Mov. Disord. 2002;17:853-66, Arch. Neurol. 2001;58:225-30), epilepsy, nystagmus, palatal tremor, and brainstem dysfunction.

The presence of GAD antibodies suggests a possible autoimmune pathogenesis of the neurologic syndrome. Sometimes, though, the neurologic syndrome occurs in the setting of insulin-dependent diabetes that by itself may be tied to the antibodies.

The question, then, is: Do GAD antibodies from patients with stiff person syndrome (SPS) and other syndromes present a different specificity from diabetic patients?

SPS patients have very high GAD antibody titers, compared with diabetes patients. Some studies claim that GAD antibodies in diabetes could be distinguished from those in SPS because the latter recognize linear epitopes, identified by immunoblot.

We reviewed the clinical features of patients with neurologic syndromes and high GAD antibody levels, arbitrarily defined as those that can be detected by immunohistochemistry and correspond to values greater than or equal to 2,000 U/ml (Brain 2008;131:2553-63). High GAD antibody levels were seen in 50 patients with neurologic symptoms.

SPS patients have very high GAD antibody titers, compared with diabetes patients. Some studies claim that GAD antibodies in diabetes could be distinguished from those in SPS because the latter recognize linear epitopes, identified by immunoblot. We reviewed the clinical features of patients with neurologic syndromes and high GAD antibody levels, arbitrarily defined as those that can be detected by immunohistochemistry and correspond to values greater than or equal to 2,000 U/ml (Brain 2008;131:2553-63). High GAD antibody levels were seen in 50 patients with neurologic symptoms.



Dr. Francesc Graus and Dr. Albert Saiz found GAD antibodies in patients with epilepsy, myasthenia gravis, and idiopathic limbic encephalitis.

Twenty-two had SPS, 17 had cerebellar ataxia, and 11 had other disorders. Four had epilepsy, 4 had paraneoplastic neurologic syndromes, 2 had idiopathic limbic encephalitis, and 1 had myasthenia gravis. The frequency of increased intrathecal synthesis of GAD antibodies was 85% in SPS, 100% in cerebellar ataxia, and 86% in other neurologic disorders. Similar GAD antibody levels were found in 11 patients with diabetes without neurologic complaints. These patients represented less than 1% of the diabetics in whom tests for GAD antibodies were requested at diabetes evaluation. In addition, the GAD antibodies of these 11 patients recognized linear epitopes like those of patients with SPS.

Our interpretation is that although the sole presence of high levels of GAD antibodies probably suggests an immunomediated underlying neurologic syndrome, they could just reflect the presence of associated diabetes or other en-

docrine disorders. However, the high frequency of a specific intrathecal synthesis of GAD antibodies in our patients supports the relation of GAD antibodies with the neurologic syndrome (Neurology 2001;57:780-4).

Another finding was that GAD autoimmunity may be related to cancer in some patients. Two of our patients had intrathecal synthesis of GAD antibodies and the tumors expressed GAD.

Detection of GAD antibodies is strong evidence that the associated neurologic syndrome may have an autoimmune pathogenesis, particularly when an intrathecal synthesis of GAD antibodies is demonstrated. However, it is unclear whether GAD antibodies are pathogenic because they enter the neuron in vivo and impair the synthesis of  $\gamma$ -aminobutyric acid. Autopsy studies of patients who had SPS or cerebellar ataxia and GAD antibodies have not demonstrated lymphocyte infiltrates to support a possible T cell-mediated damage.

ed damage.

On the other hand, when IgG isolated from patients who had GAD antibodies plus SPS or cerebellar ataxia was injected into the cerebellum and spinal cord of mice, neurophysiological and neurochemical changes were induced that were not observed after injection of IgG from GAD antibodies-positive individuals who had no neurologic symptoms. Similar results have been reported with IgG from a patient with SPS and antiampiphysin antibodies, suggesting that the SPS is directly caused by the effect of antibodies on spinal cord neurons (Ann. Neurol. 2007;61:544-51).

Our study emphasizes several points. First, high levels of GAD antibodies are associated with syndromes besides SPS. Second, GAD antibodies may just reflect concomitant diabetes or other endocrine autoimmune disorders. The demonstration of a positive intrathecal synthesis of GAD antibodies is important to confirm that the GAD autoimmunity is related to the neurologic syndrome and the patient merits consideration for immunotherapy. Third, cerebellar ataxia, the second most common syndrome associated with high GAD antibodies, shares with SPS demographic, clinical, and immunologic features.

Finally, in those patients with neurologic syndromes that suggest a paraneoplastic origin, the finding of GAD antibodies does not rule out this possibility. Studies should be done to confirm an underlying cancer. ■

DR. SAIZ and DR. GRAUS are both with the Service of Neurology, Hospital Clinic, Barcelona, Spain.

## Case Study: Anterior Choroidal Artery Infarct

BY BRADLEY J. ROBOTOM, M.D.,  
JOSE CABASSA, M.D., MARCELLA  
WOZNIAK, M.D., PH.D., AND  
STEPHEN G. REICH, M.D.

**A**n 83-year-old man presented with left-sided weakness. Examination revealed a left homonymous hemianopsia, left hemiparesis affecting face and arm, and left hemihypesthesia with intact graphesthesia and stereognosis. Magnetic resonance imaging showed an area of restricted diffusion corresponding to an infarct in the distribution of the anterior choroidal artery.

Anterior choroidal artery infarcts are uncommon; they account for just 3% of ischemic stroke, according to one study (Acta Neurologica Scandinavica, 2008;118:42-47). It was first

described by the French neurologist Charles Foix (1882-1927). It consists of a triad of hemiparesis, hemihypesthesia, and hemianopsia without cortical sensory deficits.

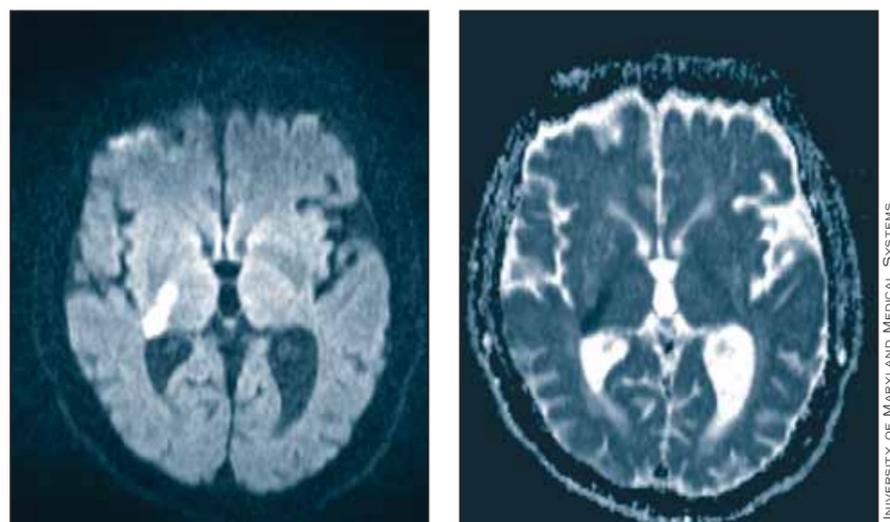


BRADLEY J.  
ROBOTOM, M.D.

Etiologies that were commonly seen in Dr. Palomas's study included large-artery atherothrombotic (38.1%), cryptogenic (38.1%), small-artery (14.3%), cardioembolic (4.8%), and coexistence of two causes (4.8%).

Increased awareness of anterior choroidal artery syndrome will enhance bedside diagnostic accuracy and help differentiate anterior choroidal artery infarcts from other stroke syndromes. ■

The authors are from the University of Maryland, Baltimore, Md., U.S.A.



Diffusion weighted imaging (left) and corresponding apparent diffusion coefficient map (right), demonstrating acute infarction: The territory supplied by the anterior choroidal artery can include the posterior limb of the internal capsule, choroid plexus, initial segments of the optic radiations, and parts of amygdala, uncus, and globus pallidus.

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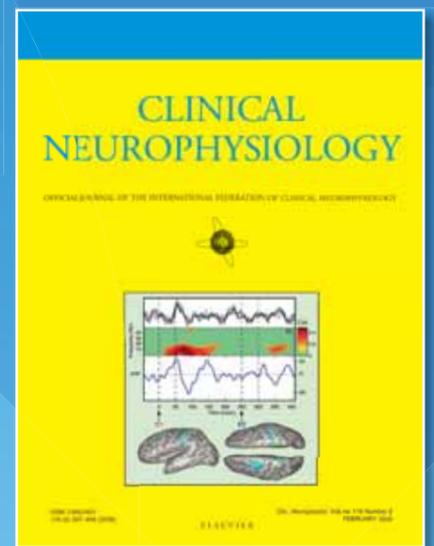
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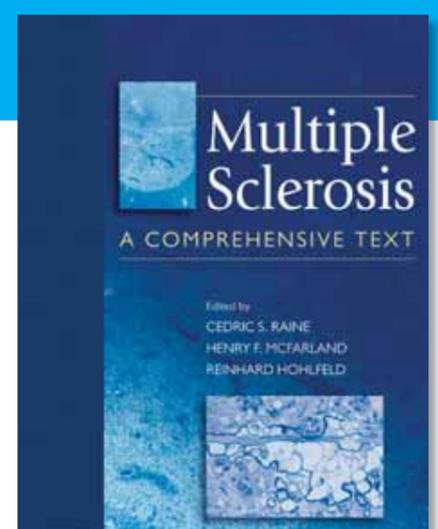
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## Edwin Robert Bickerstaff: 1920-2008

BY DAFYDD THOMAS, M.D.

**D**r. Edwin Robert Bickerstaff has died at the age of 87. He was one of the outstanding clinical neurologists of the 20th century.

Dr. Bickerstaff was born on November 20, 1920, in Wales. His father was High Sheriff of Cardiganshire and a governor of the University College of Wales in Aberystwyth. Dr. Bickerstaff was educated at King Edward's School in Edgbaston, Birmingham. He had a fine singing voice, and he had to decide between a career in music or medicine. He joked that he was not robust enough for the former, so chose the latter; so much the better for his many patients and students.

He qualified MB, ChB at the University of Birmingham's Medical School in 1943. He joined the Royal Air Force and was involved in the Normandy invasion. He was appointed squadron leader and ran the RAF's tuberculosis service. He presented his MD thesis on TB in 1947. He returned to Birmingham to continue his training and soon developed an interest in neurology.

In 1952, Dr. Bickerstaff had an inspirational year with Dr. Raymond Adams, then chair of neurology at Massachusetts General Hospital, Boston and a pioneer in stroke research. On returning to Birmingham, Dr. Bickerstaff was appointed senior registrar and then promptly consultant neurologist to the Midland Centre for Neurosurgery and Neurology (MCNN),



COURTESY SARA BICKERSTAFF

**Early on, Dr. Bickerstaff chose a career in medicine over a singing career.**

where he loyally remained until his retirement from the Health Service in 1985.

The MCNN served 8 million patients. He built up its clinical and diagnostic services and its reputation. Despite being senior neurologist, his clinical workload remained huge with regular clinics in the West Midlands, Coventry, Hereford, and Shrewsbury. The first time I filled in for him at his Friday afternoon clinic in Shrewsbury, there were 20 new outpatients and 15 ward referrals at three different hospitals.

Dr. Bickerstaff's powers of observation, analysis, memory, and his high level of energy were legendary. He said he learnt from every patient he saw. Dr. Bickerstaff's opinion was more valuable the more

knowledgeable one became. He was extremely well organized; little clinical information was wasted.

Early on, Dr. Bickerstaff started using a punched-card system: A staff member completed a card for every inpatient and outpatient seen by him or his senior registrars. It was a system that enabled Dr. Bickerstaff to retrieve and collate diagnostic groups rapidly. Through this punched-card system, Dr. Bickerstaff was able to detect the differences in the neurologic problems arising in young women in the 10 years before and after the introduction of oral contraceptives to the marketplace. His book, *Neurological Complications of Oral Contraceptives*, published by Oxford University Press to acclaim in 1975, is still worth reading. Indeed, his prose is worthy of Jane Austen. He covered not only cerebral arterial and venous thromboses but also chorea, migraine, and control of epilepsy in women taking oral contraceptives.

Another book, "Neurological Examination in Clinical Practice," in 1963, became a classic with six editions over 25 years. His textbook, "Neurology for Nurses" had four editions over 20 years.

But Dr. Bickerstaff was primarily a clinician. He was appointed honorary senior lecturer for his brilliant teaching of students and postgraduates but had no paid academic sessions. All his research and writing were done in his spare time.

Dr. Bickerstaff's main interests were cerebrovascular disease, particularly in children. He was consultant to Birmingham's Children's Hospital. Other areas of clinical interest were young adults, migraine, and infections of the nervous system. He made significant contributions to the literature on each topic. "Basilar migraine," where consciousness may be lost in a migraine attack, without an epileptiform event, will always be associated with him. His 1957 BMJ paper, "Brain-stem encephalitis—further observations on a grave syndrome with benign prognosis," will ensure that his name will survive (*Br. Med. J.* 1957;1:1384-7).

Dr. Bickerstaff became president of the neurologic section of the Royal Society of Medicine. The Danish and French neurologic societies elected him an honorary member. He led the Midland Neurological Society and was a trustee and council member of the Association of British Neurologists. His attendance and contributions continued long after his retirement.

During retirement, Dr. Bickerstaff was able to indulge his interest in music and literature. He spent many happy hours on the golf course, until the onset of a non-dominant hemisphere stroke 2 years ago.

He is survived by his devoted wife, Sara, and two children, Peter and Helen, from his first marriage, four grandchildren, and four great-grandchildren.

*Da iawn,*

*Diolch yn fawr, 'Dwin.* ■

DR. THOMAS is professor emeritus of clinical neuroscience at the Imperial College, London.

## Wayne Alfred Hening: 1945-2008

BY ARTHUR S. WALTERS, M.D.

**D**r. Wayne Alfred Hening born on Jan. 29, 1945, passed away from pulmonary fibrosis on Sept. 15, 2008.

He obtained his MD from New York University School of Medicine in 1978 and completed his internship at Stanford (California) University in 1979. In 1982, Dr. Hening completed both his neurology residency and his PhD at Columbia Presbyterian Medical Center, New York. His mentor there was Dr. Eric R. Kandel, who, in his acceptance speech for the 2000 Nobel Prize in Physiology and Medicine, praised Dr. Hening's early work on the *Aplysia* (sea slug) as a model of more complex human neuronal and behavioral functioning.

Dr. Hening also trained as a movement disorder fellow with Dr. Stanley Fahn of Columbia Presbyterian from 1982 to 1984 and remained there 2 more years as a postdoctoral fellow of Dr. Claude Ghez to complete an experimental study on motor control.

With movement disorders as a background, Dr. Hening later became certified in sleep medicine. Dr. Hening combined these two interests in a brilliant way and helped establish the field of sleep-related movement disorders. Much of this work was done at the University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School, Camden and the Lyons Campus of the New Jersey

Health Care System, where he joined his frequent coauthors, Dr. Arthur Walters and Dr. Sudhansu Chokroverty, in 1986.

He was coeditor of the first book on sleep-related movement disorders in 2003. He was one of the key individuals who helped establish the essential diagnostic clinical criteria for restless legs syndrome (RLS), first published by the International Restless Legs Syndrome Study Group (IRLSSG) in 1995. He was one of the key individuals who helped create and validate the first severity rating scale for RLS that is now used as the primary end point in all major trials of pharmacotherapeutic agents for the treatment of RLS. He was the first in 1999 to establish that the symptoms of RLS are triggered by an underlying circadian rhythm. He was also the first to point out that there are mimics of true RLS that superficially meet the minimal diagnostic criteria for RLS. He was among the first in 1986 to do a polysomnographic study on RLS documenting the therapeutic effect of opioids, and he was coauthor in 1988 on the first double-blind polysomnographic studies of a dopamine agonist and in 1993 on an opioid agonist in RLS. Most recently, he worked at the RLS center at Johns Hopkins University, Baltimore, with Dr. Richard Allen and Dr. Chris Earley. There, Dr. Hening was key in establishing and validating the first telephone diagnostic interview for the symptoms of RLS and where he con-



COURTESY DR. WALTER PAULUS

**Dr. Hening was a pioneer in the field of sleep-related movement disorders.**

ducted a large study of the relatives of RLS patients, the first of its kind.

Dr. Hening was the principal person responsible for writing the bylaws of both the IRLSSG and the World Association of Sleep Medicine (WASM). He served as the current secretary of the IRLSSG, as an associate editor of sleep medicine, and as head of the sleep section of the American Academy of Neurology. PubMed lists him as having 95 publications, 55 of which were in the last 8 years of his life with several more to be published posthumously.

Dr. Hening was comfortable in any social situation in any culture. He had friends from all around the world. He sought out such friendships and he main-

tained them. Dr. Hening would seek out young people and encourage them to enter the field of sleep-related movement disorders research. He would then generously give of his time to these young people. Dr. Hening was happy to give them first authorship on publications and many times he refused authorship even though he had made significant contributions to the planning and design of the research. The growth and prospering of the field was his reward. On his extensive travels, he took his ready smile and a great sense of humor; they were useful assets as he helped coordinate research activities all around the world in the field of RLS. Dr. Hening was a connoisseur of fine food and wine, and seemed to know the best restaurant in most cities no matter where in the world he found himself. Dr. Hening was well read in history, literature, economics, music, culture, and philosophy, and he leaves behind some excellent poetry as well. One of his favorite activities was organizing a trip to the finest restaurant in any city with a large group of new and old friends alike. The field of sleep-related movement disorders has lost a true pioneer and contributor and a fine friend and human being as well. He will be deeply missed by us all. ■

DR. WALTERS is professor of neurology, Vanderbilt University Medical School, Nashville, Tenn., U.S.A.

## Profile: Marianne de Visser, WFN Trustee

BY MARIANNE DE VISSER, M.D.

I have served two full terms on the management board of the WFN. The first 3 years were under President Jun Kimura and from 2005 on under President Johan A. Aarli.

Each president was unique. Dr. Kimura was an inspiring personality with a wonderful sense of humor. He restructured WFN, paved the way for the membership of the Republic of China, and greatly supported the educational committee which reached out to neurologic societies in countries with poor resources by providing them with educational material—continuum in particular, donated by the American Academy of Neurology.

During Dr. Jun's presidency, Dr. Aarli was vice president. He was the driving force behind WHO's initiative to draw up an atlas encompassing worldwide information about neurologic resources. Although it was no surprise, the atlas showed a dramatic lack of neurologic care in Africa.

As president, Aarli worked with several African neurologists to change that situation. One of them, Senegalese neurologist Gallo Diop, is the prototype of an authoritative and inspiring leader. He showed us that there is great potential in Africa, but that there is a need for support, especially regarding continuous medical education.

I qualified in medicine at the Municipal University of Amsterdam and trained in neurology at the Wilhelmina Gasthuis in Amsterdam. There I was inspired by Prof. Jaap Bethlem, the pioneer in neuromuscular diseases in the Netherlands who set up the first one-stop diagnostic shop. He inspired numerous residents to do research in this field. I joined his group and wrote a thesis on the phenotype of Becker muscular dystrophy. Subsequently, I became a member of the staff of the department of neurology at the Wilhelmina Gasthuis, which later moved to the Academic Medical Center, Amsterdam. In 1985, I succeeded Prof. Bethlem after his retirement and became professor of neuromuscular diseases at the University of Amsterdam.

From 1989 to 1997, I served on the board of directors of the Netherlands Society of Neurology and eventually became president. I was appointed delegate and attended the annual meetings of the WFN council of delegates, where I faced the fundamental problems of countries without neurologists. The mission of the WFN was very appealing and extremely challenging, and therefore I decided to stand for election to the position of elected trustee.

In professional life, I gradually shifted my attention to hereditary neuropathies and inflammatory myopathies. In collaboration with geneticists Piet Bolhuis and Frank Baas, we identified the first mutations in the demyelinating form of Charcot-Marie-Tooth disease and the unraveling of the genetic defect in the collagen VI gene as the cause of Bethlem myopathy.

At the Academic Medical Center, amyotrophic lateral research had been the focus of research for decades, first by Prof. A. Biemond and his group and later by Prof. den Hartog Jager and Prof. Vianney de

Jong. Prof. De Jong was dedicated to his patients, and collected an impressive cerebrospinal tissue bank that provided a unique resource for research. After he retired, with colleagues at the University of Utrecht and University of Nijmegen (both in the Netherlands), we established the ALS Center.

I should like to thank the WFN trustees for their friendship and encouragement, the London office for their professional support, and the the membership committee for their critical appraisal of the applications of the national societies. ■

DR. DE VISSER is professor of neurology at the Academic Medical Center, Amsterdam.

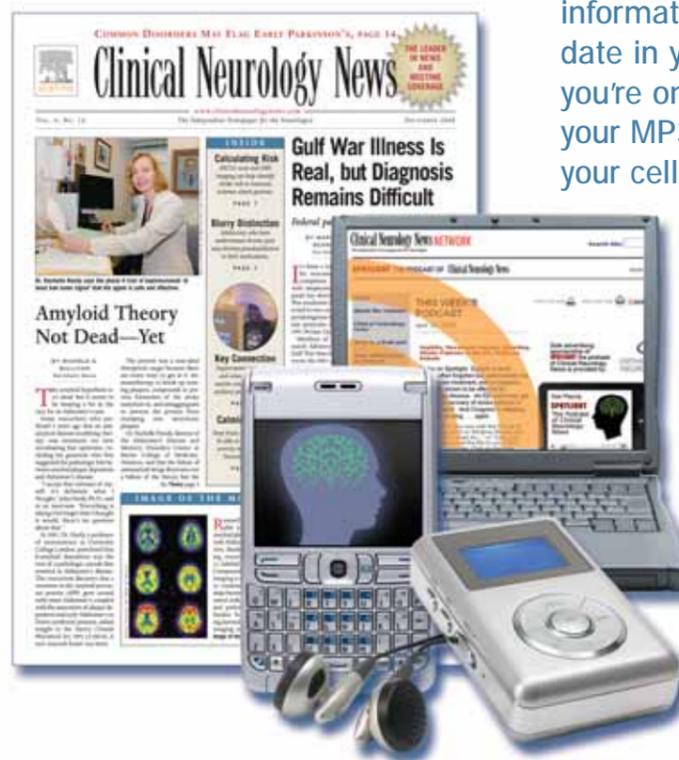


Dr. de Visser has found the mission of the WFN both appealing and challenging.

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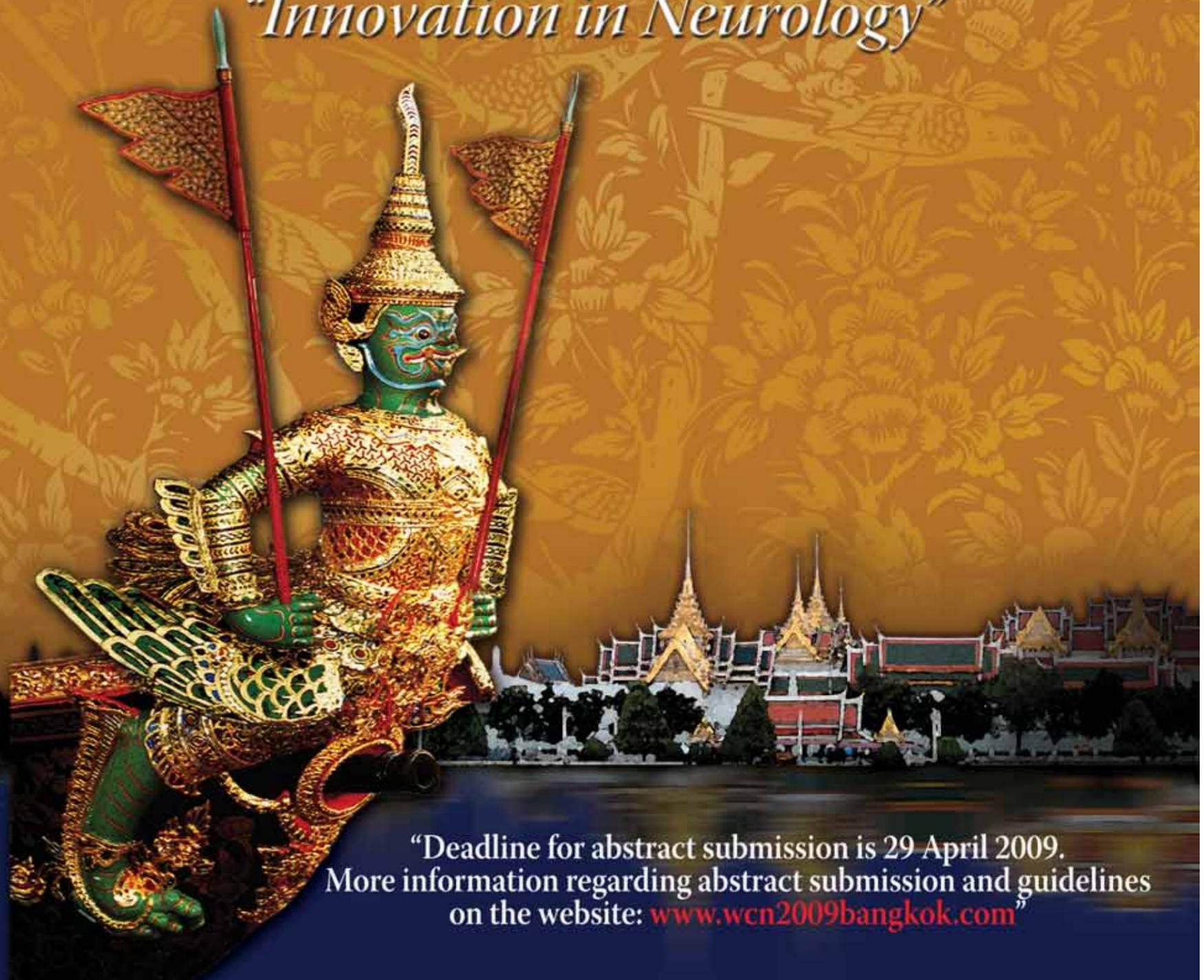
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