

# WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

## Unity Defines Council of Delegates' Meeting

BY MARK HALLETT, M.D.  
*Editor in Chief*

The annual general meeting of the World Federation of Neurology's Council of Delegates was held Sept. 26 in Geneva, during the 14th congress of the European Federation of Neurological Societies (EFNS). Right from the start, there was a show of unity within our international community when, during the roll call, it was announced that the delegate from Taiwan, Ching-Piao Tsai, had the proxy from China.

Vladimir Hachinski, president of the World Federation of Neurology, greeted the delegates warmly and introduced the central topics of the meeting. His main message was that work was proceeding well on all fronts, that the WFN was on stable financial footing, that projects were going forward with limited funding, and that he welcomed more involvement of the delegates in Federation business. He noted in particular that the plans for the World Neurology Congress to be held Nov. 12-17, 2011, in Marrakesh, Morocco, were progressing very nicely. In addition to the elected trustees, the officers have appointed Donna Bergen and Stephen Sergay, both of the United States, as co-opted trustees.



Adel Misk, left, of the Palestinian Neurological Society, and Hesham Awn, right, of the Yemeni Neuroscience Society. Their societies were elected new members of the WFN.

Vice President Werner Hacke (Germany) said that the WFN Web site was being modernized, even though it was already considered a high-quality site. Pete Engel (USA) is the new Web editor, and the plan is to add much more educational content. The WFN will hire a professional Web design and management company to ensure that the site is user-friendly and accessible.

Education Committee cochairs Dr. Sergay and Wolfgang Grisold (Austria) de-

scribed an active program to develop more educational material. They introduced Riadh Gouider (Tunisia) and Morris Freedman (Canada), cochairs of the e-learning task force, who are developing material for the site in conjunction with their counterparts on an EFNS task force.

In a report on the Africa Initiative, Alfred K. Njamshi (Cameroon), the regional director for Pan Africa, said the initiative continues to focus on conducting educational courses and training across the continent. He noted the EFNS and International Brain Research Organization's valuable support and contribution in planning and presenting the courses. The University of Cairo is now signing a memorandum of understanding with the WFN to arrange for neurology residents from other African countries to train at that institution. Past-President Johan Aarli, who began the Africa program during his

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In 25 years, neurology has grown from a small, underresourced specialty into one with excellent training and care centers and improved patient access to treatment.

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#### Kazakhstan

We introduce the League of Neurologists of Kazakhstan, a new member of the WFN community, and learn about the state of the specialty in that country.

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## Multiple Sclerosis Disease Activity May Vary Seasonally

BY JEFF EVANS  
*Elsevier Global Medical News*

Disease activity on MRI in multiple sclerosis patients is most likely to occur and is most intense in the spring and summer, according to a retrospective, observational study of a 3-year period in Boston.

Although the rates of clinical attacks and new contrast-en-

hancing lesions were not associated with significant seasonal differences, new T2 lesions developed in the spring and summer at nearly twice the rate as in the fall and winter. This finding "may raise concerns for design and analysis of clinical trials with MRI outcome measures. If left unaccounted this effect could bias longitudinal assessment both at individ-

ual as well as group level," wrote Dominik S. Meier, Ph.D., of Brigham and Women's Hospital, Boston, and colleagues.

The findings agreed with previous studies that measured the seasonality of clinical markers in Japan, Sweden, and the United States (Ohio and Arizona). Another three studies that have examined MRI markers across the seasons had biased inclu-

sion criteria or poor longitudinal follow-up, according to the investigators.

They matched meteorological data with clinical data from 44 patients who underwent 939 brain MRI scans during 1991-1993. The cohort included 13 patients with chronic progressive MS and 31 with relapsing-remitting MS. They had a mean age of 38 years, a mean disease

duration of 8 years, and a mean Expanded Disability Status Scale score of 3.9.

Each patient underwent eight weekly scans, followed by eight scans every other week and six monthly examinations. No patient received disease-modifying therapies (Neurology 2010; 75:799-806).

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JOURNAL OF THE  
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Editor

Applications are invited for the editorship of this leading peer-reviewed journal, which publishes research articles in all areas of the neurological sciences. See Page 11

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## EDITOR IN CHIEF'S COLUMN

## Working Together

One of the striking characteristics of the Council of Delegates meeting that I have reported on in the lead article in this issue is the cooperation among the different countries. That China gave its proxy to Taiwan and that the delegate from Israel moved the acceptance of the Palestinian Neurological Society were two manifestations of the community of neurologists working together for common goals.

With all the tensions in the world, all those factors that divide people, it is certainly nice to see that on some level people can work together. I won't enumerate the factors that divide, but sometimes they appear to be superficial and political. The common folks, like us neurologists, are friendly and have a similar purpose: to prevent neurological disease and to improve the lives of our patients.

There is also cooperation among societies. The American Academy of Neurology supplies copies of *Continuum* that can be used as educational material in developing countries. The International Brain Research Organization and the European Federation of Neurological Societies have cooperated with the World Federation of Neurology in running many training courses in neuroscience and neurology in Africa.

And, of course, the individual na-

tional neurological societies are cooperating with each other in many different ways and combinations within the umbrella of the WFN.

If only it were possible to generalize this cooperation even more. Every little bit helps, and it is worthwhile to spread the good news when it happens.

The main goal of the WFN, in pursuit of better patient care, is clearly the education of neurologists. There are plans to have more educational material on the WFN Web site, e-learning activities, regional courses, development of residency training programs, and, of course, the Federation's biennial world congresses that will come to various parts of the world.



BY MARK HALLETT, M.D.

Neurological disorders are on the increase – head trauma, stroke, Alzheimer's disease, Parkinson's disease, and other disorders. The need for neurologists outstrips the supply, and clever ways to increase neurological care have been developed (and emphasized from time to time in *WORLD NEUROLOGY*). We will also need research, not only for improved treatments, but also for better ways of delivering patient care. The WFN has not been able to embrace much research as yet, but perhaps some of the currently available seed money could be used to support such work. Certainly, we would anticipate excellent cooperation from all involved. ■

## Calendar of International Events

## 2011

**4th European Neurological Conference on Clinical Practices**  
Jan. 28-30  
Lisbon, Portugal  
[www.paragon-conventions.net/encpc2011](http://www.paragon-conventions.net/encpc2011)

**10th International Conference on Alzheimer's & Parkinson's Diseases**  
March 9-13  
Barcelona, Spain  
[www.kenes.com/adpd](http://www.kenes.com/adpd)

**3rd Asian and Oceanian Parkinson's Disease and Movement Disorders Congress**  
March 25-27  
Taipei, Taiwan  
[www.aopmc2011taiwan.com/index2.html](http://www.aopmc2011taiwan.com/index2.html)

**63rd Annual Meeting of the American Academy of Neurology**  
April 9-16  
Honolulu, Hawaii, USA  
[www.aan.com/go/am11](http://www.aan.com/go/am11)

**9th European Paediatric Neurology Society Congress**  
May 11-14  
Cavtat-Dubrovnik, Croatia  
[www.epns2011.com](http://www.epns2011.com)

**20th European Stroke Conference**  
May 24-27  
Hamburg, Germany  
[www.eurostroke.eu](http://www.eurostroke.eu)

**21st Meeting of the European Neurological Society**  
May 28-31  
Lisbon, Portugal  
[www.congex.ch/ens2011](http://www.congex.ch/ens2011)

**Movement Disorder Society 15th International Congress of Parkinson's Disease and Movement Disorders**  
June 5-11  
Toronto, Canada  
[www.movementdisorders.org/congress/congress11](http://www.movementdisorders.org/congress/congress11)

**European Neuro-Ophthalmology Society Meeting**  
June 18-21  
Barcelona, Spain  
[www.eunos2011barcelona.com](http://www.eunos2011barcelona.com)

**World Congress on Huntington Disease**  
Sep. 11-14  
Melbourne, Australia  
[www.worldcongress-hd2011.org](http://www.worldcongress-hd2011.org)

**Asia Pacific Stroke Conference**  
Sep. 29-Oct. 1  
Colombo, Sri Lanka  
[www.apsc2011.com](http://www.apsc2011.com)

**7th International Congress on Vascular Dementia**  
Oct. 20-23  
Riga, Latvia  
[www.kenes.com/vascular](http://www.kenes.com/vascular)

**20th World Congress of Neurology**  
Nov. 12-17  
Marrakesh, Morocco  
[www2.kenes.com/wcn/Pages/Home.aspx](http://www2.kenes.com/wcn/Pages/Home.aspx)



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## PRESIDENT'S COLUMN



BY VLADIMIR  
HACHINSKI, M.D.

## Change, Continuity, Now Implementation

**F**estina lente, make haste slowly, admonished Emperor Augustus. That's easier said than done in our texting-, blogging-, tweeting-obsessed world, and yet it remains sound advice.

The current administration was elected on a platform of continuity and change. Educational programs and teaching courses are continuing, the *Journal of Neurological Sciences* is doing well scientifically and financially, *WORLD NEUROLOGY* is heading toward new heights, as are the World Congresses.

My proposal as Vice President in 2001 that the World Congress of Neurology be held every 2 years was greeted with both enthusiasm and skepticism. We chose to "make haste slowly" and evaluate the options on the premise that hard thinking leads to easy implementation. It is already evident that the move to biennial congresses has resulted in greater continuity in the organization of the Congresses and the composition of the Scientific Program Committee, with resulting efficiency and an increased income from the more frequent Congresses.

The approach of systematic evaluation and priority setting is serving the administration well. We began with an inventory of all our activities by establishing the value of a current or proposed activity, its viability, its potential for synergy within the WFN and with other organizations, and how it will be evaluated.

This process took place largely through e-mail and conference calls. During the annual meeting of the American Academy of Neurology in Toronto in April, a number of Delegates and Committee Chairs, and the Chairs of the Initiatives and Task Forces, were able to convene with the Trustees and each other. In July, we gathered in London for a Strategic Planning and Pri-

ority Setting Retreat at which the WFN leaders got to know each other and learn about their respective priorities. Information can be exchanged quickly; trust, collegiality, and a sense of common purpose take a bit longer to build ... *Festina lente!*

Finally, in September, we held our annual Council of Delegates' meeting at the European Federation of Neurological Sciences in Geneva.

Chris Kennard, Chair of the Publication Committee, reported on the outstanding job that Robert Lisak has done as Editor of the *Journal of the Neurological Sciences*. During Dr. Lisak's unprecedented three terms, the journal's impact factor has increased steadily, its quality improved, and its profitability has edged upward. Dr. Lisak graciously agreed to continue his editorship until a successor has been appointed. **The position for Editor is advertised on page 11 of this issue of *WORLD NEUROLOGY*.**

Mohammad Wasay, Chair of the Public Awareness and Action Committee shared his plans for involving the media in neurological campaigns and has invited a former advertising executive to be part of the Publications Task Force.

Aksel Siva, Chair of the Task Force on Standards and Branding, and his Cochairs, Sarosh Katrak and Charles Warlow, have produced a set of criteria for the endorsement of neurological meetings and congresses, with the focus being on value and quality.

Werner Hacke, Chair of the Congress Supervisory Committee, and El Mostafa El Alaoui Faris, President of the 20th World Congress of Neurology, gave a progress report on planning for the Congress in Marrakesh on Nov. 12-17 next year. The WFN leadership also met with the Austrian Society of Neurology, hosts of the 2013 Vienna WCN, and worked out an equitable profit-sharing plan. It includes the EFNS, which is foregoing its 2013 annual meeting in the spirit of collegiality and commitment to world neurology.

At the end of the 3 days of WFN meetings, the Trustees held a synergium with the attendees. "Synergy" the concept, became "synergy" the action, and the sense of collegiality and common purpose that was stirred at the London Retreat bloomed and flourished in Geneva. *Festina lente* has been worthwhile!

As Mark Hallett writes in his column and lead story, the cooperation and exchange between the delegates reflected the extent to which WFN neurologists are willing to work together for a common cause, despite prevailing political tensions between some of their countries. For example, a land dispute dating back to the 19th century between Bolivia and Chile simmers to this day, yet the Chilean Delegate, Renato Verdugo Latorre, brought the proxy vote of his Bolivian counterpart, Juan Carlos Duran. Some years back, President John Aarli and Secretary-Treasurer General Raad Shakir negotiated a way to comply with the "one-China policy" without expelling Taiwan. They created a China Region of the WFN comprising Taiwan, Hong Kong, and China, each with one vote. This September, Ching-Piao Tsai, President of the Asian and Oceanian Association of Neurology and Delegate of Taiwan, carried the proxy for Chuan-Zhen Lu from China. Natan Bornstein, Delegate for Israel, proposed the Palestinian Neurological Society for WFN membership.

Having planned change on a baseline of continuity and stability, we are ready to move ahead in the coming year at an accelerated pace. **The WFN is inviting applications for projects through the different Committees and Task Forces. Terms of reference, the process, and deadlines will be posted on the Web site in early 2011.**

The theme next year will be "Implementation," and the motto, inspired by the Roman poet Virgil, will be *Audaces fortuna iuvat* – fortune favors the bold.

My very best wishes to you all for the holidays and a healthy, successful, and synergistic New Year! ■

## NEUROLOGICAL PEARL

## Sorting Out the Marcus Gunn Phenomena

BY AINHI HA, B.SCI. (MED.),  
B.MED./B.SURG., AND JOSEPH  
JANKOVIC, M.D.

**R**obert Marcus Gunn, a Scottish ophthalmologist (1850-1909) trained at the University of St. Andrews and University of Edinburgh. He served as a senior surgeon at the Moorfields Eye Hospital in London and president of the Ophthalmological Society of the British Medical Association. He produced a series of unique ophthalmological and neurological observations.

► **Marcus Gunn phenomenon.** Also known as Marcus Gunn jaw-winking synkinesis, this condition refers to the retraction of eyelid ptosis that occurs with jaw opening.

It affects about 5% of congenital cases of ptosis<sup>1</sup> and is thought to result from misdirected innervation of trigeminal nerve branches into the levator palpebrae superioris muscle.<sup>2</sup> Electrophysiological studies reveal evidence of levator and pterygoid cocontraction.<sup>3</sup>

Individuals with the condition require ophthalmological surveillance because of the risk of complications, including strabismus, amblyopia, and anisometropia.

► **Marcus Gunn pupil.** This refers to the abnormal pupillary response seen with a relative afferent pupillary defect in the setting of optic nerve atrophy.

In 1902, Gunn described the phenomenon of pupillary redilation under sustained illumination.<sup>4</sup> Levatin further described the swinging light test in 1959,<sup>5</sup> which may be considered a modification of Gunn's technique.<sup>6</sup> Recognition of Marcus Gunn pupil is particularly valuable in assessing patients for multiple sclerosis because it may be present even without prior clear history of optic neuritis.

► **"Marcus Gunn sign."** In 1897, Gunn described the four cardinal retinal signs of arteriolar sclerosis:<sup>7</sup> tortuosity of the arteries; variation in caliber of the vessels; alteration of the normal light streak; and indentation of the veins at the arteriovenous crossings. He is

credited as one of the first to suggest these changes were not solely attributable to aging.<sup>7</sup>

► **Gunn's dots.** These retinal dots, also known as Crick dots,<sup>8</sup> are likely of no clinical significance.

► **Inverted Marcus Gunn phenomenon.** This rare condition is also referred to as Marin Amat syndrome. It involves simultaneous eye closure with jaw opening, in contrast to the eye opening seen in the Marcus Gunn phenomenon.

The Spanish ophthalmologist Marin Amat described this sign in 1918, although earlier reports of it had been published by Müller-Kannberg in 1894 and Higier in 1902, according to Wartenberg.<sup>9</sup>

It is typically seen after a peripheral cranial nerve injury. One possible mechanism is aberrant reinnervation involving the trigeminal and facial nerve. Wartenberg postulated that orbicularis oculi contraction occurred in the setting of facial muscle activity, rather than activation of the trigeminal nerve, based on the observation of eye closure only with extensive

mandibular movement (associated with secondary facial muscle activation).<sup>9</sup> ■

DR. HA is a movement disorders fellow at the Parkinson's Disease Center and Movement Disorders Clinic, department of neurology, Baylor College of Medicine, Houston, USA. DR. JANKOVIC is a professor of neurology and the director of the Parkinson's Disease Center and Movement Disorders Clinic.

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## WFN EDUCATION COMMITTEE

# Working to Provide Neurological Training for Generalists

There are at least 250 million people with brain disorders in the developing world, yet in many regions there is a severe shortage of neurological health care services.

Patient:neurologist ratios generally fall well below the suggested 1 neurologist per 100,000 population; a large study on neurological services in Africa, for example, reported that 23 of the continent's 53 nations averaged 1 neurologist per 5 million population (Neurology 2005;64:412-5). In addition to the shortage of neurologists, imaging and diagnostic facilities are more often than not scarce, underresourced, or non-existent.

Given these restrictions, general practitioners (GPs), especially those working in remote rural areas, have to pick up the neurological disease burden.

They need to know how to diagnose, treat, and manage neurological disorders and when to use resources to transport patients for specialized neurological care – and to do that, they need training. However, training projects may be hampered because of limited funding and resources.

The World Federation of Neurology (WFN) is working to find ways to offset the shortage of neurologists by providing neurological education for GPs. I am a member of the Education Committee and in charge of undergraduate and non-neurologist education in developing countries, and through this article, I hope to raise awareness of this shortage of neurologists, describe possible ways of improving general-

ist neurological training, and seek your support and recommendations on how we can proceed.

This is what my colleagues and I are thinking at the moment: We would like to establish a database of curricula and teaching resources for neurological educators to access on the WFN Web site and to set up a Web-based forum so that the educators can share and develop teaching strategies.

Core neurology e-texts – such as the symptoms-based approach to neurological complaints by the American College of Physicians and the American Academy of Neurology – would be made available to GPs. The joint ACP-AAN multimedia tool, Approach to Common Neurological Symptoms in Internal Medicine ([www.aan.com/go/education/curricula/internal/toc](http://www.aan.com/go/education/curricula/internal/toc))

was designed to improve neurological knowledge at the undergraduate and postgraduate levels and would be a valuable resource for generalists who practice in remote rural areas.

Other useful neurology e-texts and Web links, such as those to AAN practice guidelines and medication information, would all help in disseminating information to GPs.

There are several ways in which we could promote neurological learning in remote locations. Web-based resources could be used, depending on the availability of computers and Internet connectivity, or discs and videos with neurological information could be distributed to areas where connectivity is a problem. We also

need to have more detailed modules on common and dangerous neurological disorders that occur in developing countries.

Another possibility would be to have a Web-based forum where GPs can discuss patient cases with a practicing neurologist. Case-based learning through phone consultations with a neurologist is another extremely effective teaching tool.

Neurologist Mamta Bhushan Singh has described an initiative in India called the Lifeline Express, which was established to reduce the incidence of curable or treatable conditions such as epilepsy, blindness, deafness, physical handicaps, and deformities in the country's rural areas (WORLD NEUROLOGY, August 2010, p. 1). Dr. Singh and her team participate in the program to treat epileptic patients and to provide a basic epilepsy orientation course for local doctors. Perhaps the model for this program could be applied elsewhere and adapted to address other neurological disorders.

If you have any suggestions about improving generalist neurological education, please contact me at [bscherokman@gmail.com](mailto:bscherokman@gmail.com).

We are specifically interested in help with the following:

- ▶ Undergraduate and postgraduate neurological training curricula and teaching resources.
- ▶ Availability of computers to GPs in remote locations.
- ▶ A list of the most common and dangerous disorders that occur in your country that GPs should be especially aware of.
- ▶ Ideas on providing neurological consultations for remote GPs.
- ▶ Ways in which your country is currently trying to address the shortage of neurologists. ■



BY BARBARA SCHEROKMAN, M.D.

Dr. Scherokman is a clinical professor of neurology at the George Washington University, Washington, D.C.

## Risks of Carotid Stenting Are Found To Continue in the Long Term

BY MARY ANN MOON  
Elsevier Global Medical News

Carotid artery stenting carries higher intermediate- and long-term risks than does carotid endarterectomy, not just higher periprocedural risks, according to the largest and most comprehensive metaanalysis of available evidence from randomized trials to date.

The safety and efficacy of carotid stenting as an alternative to endarterectomy are controversial. Several studies have indicated that stenting is more likely to cause periprocedural stroke, but the data on longer-term outcomes are limited, said Dr. Sripal Bangalore of New York University, New York, and his associates.

The investigators examined 13 randomized controlled trials that reported outcomes at 30 days or later and included 3,754 patients assigned to stenting and 3,723 to endarterectomy. The mean follow-up in the trials was 2.7 years.

In the short term, stenting was associated with a 31% increase in the risk of periprocedural death, MI, or stroke, compared with endarterectomy. The absolute rates of periprocedural death, MI, or stroke were 5.7% with stenting and

### VITALS

**Major Finding:** The long-term risk of stroke is 48% higher after carotid stenting than after carotid endarterectomy, and the long-term risk for the composite outcome of death or stroke is 24% higher.

**Data Source:** A metaanalysis of 13 recent randomized clinical trials comparing the two approaches and having a mean follow-up of 2 years.

4.7% with endarterectomy, they said.

In the long term, the risk for that composite outcome plus later ipsilateral stroke or death was 19% higher following stenting than it was after endarterectomy. In comparison with endarterectomy, stenting carried a 38% higher risk of the composite outcome of periprocedural stroke or death plus later ipsilateral stroke, a 24% higher risk of the composite outcome of death or stroke, and a 48% increased risk of any stroke.

These increases in long-term risks were consistent across several subgroups of patients: symptomatic or asymptomatic, low risk or high risk, American or non-American, and regardless of whether an embolic protection device was used, Dr. Bangalore and his colleagues wrote (Arch. Neurol. 2010 Oct. 11 [doi:10.1001/archneurol.2010.262]).

However, the rate of periprocedural

MI was significantly lower with carotid stenting (0.3%) than with endarterectomy (1.2%). And stenting was associated with an 85% reduction in the risk of cranial nerve injury, all of which occurred in the periprocedural period. "Our results suggest that the [already known] periprocedural increased risk of carotid artery stenting continues to be seen in the intermediate-to long-term periods as well," wrote the investigators.

Despite these findings, carotid stenting remains a useful alternative, given that it is less invasive and entails a shorter recovery period than endarterectomy and that it would be beneficial for patients who are poor surgical candidates or at high risk for periprocedural MI. Therefore, "there is an urgent need" to develop the means to select patients who have a low risk of complications with stenting, the researchers added.

**Disclosures:** One investigator reported receiving research grants from AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, HeartScape, Sanofi Aventis, and the Medicines Company. ■

## Stroke Message Of Solidarity

The search is on for a universal stroke awareness symbol for stroke.

Attendees at the 7th World Stroke Congress in Seoul in October identified primary prevention, treatment, and long-term quality care and support for stroke patients as the crucial components in fighting the disease. Also key to those efforts, noted Bo Norrvig, president of the World Stroke Organization (WSO), would be a unifying symbol to help raise awareness of the disease and spur the international stroke community to rise to the challenges of combating it.

Each year, 15 million people worldwide suffer a stroke, and 6 million people die as a result of stroke.

The WSO, known as the "voice for stroke," has launched a competition to find a symbol that will help it promote its worldwide mission and spread its lifesaving message. The concept should encapsulate the theme that "unity is strength."

To join the contest and enter your submission, go to <http://forms.worldstrokecampaign.org/2010/SymbolCompetition/>. The winner will be announced in 2011. ■



# Stroke History Did Not Alter Dabigatran Safety, Efficacy

BY JEFF EVANS

*Elsevier Global Medical News*

**P**atients with atrial fibrillation who were taking the anticoagulant dabigatran for secondary stroke prevention suffered an ischemic stroke or systemic embolism at a rate similar to patients taking warfarin in a prespecified subgroup analysis of patients from the 2-year RE-LY trial.

This analysis of 3,623 patients was consistent with the overall results found in the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) trial cohort of 18,113 patients. Significant differences in the rates of intracranial bleeding between patients treated with dabigatran and those taking warfarin that had been observed in the overall results of the trial also were seen in those with a history of ischemic stroke or TIA.

## Subgroup Variations 'Unlikely'

"Although the subgroup analyses were not powered to detect whether the effects of dabigatran compared with warfarin varied by subgroup, the overlapping 95% confidence intervals suggest that major variations in the relative effects of the drugs between the patients with or without previous stroke or transient ischemic attack are unlikely," Dr. Hans-Christoph Diener of University Hospital Essen (Germany) and his coinvestigators wrote (*Lancet Neurol.* 2010 Nov. 8 [doi:10.1016/S1474-4422(10)70274-X]).

The US Food and Drug Administration (FDA) approved the drug in October at doses of 150 mg and 75 mg for reducing the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation. The approval was based on the overall results

of the open-label RE-LY trial, which randomized patients with atrial fibrillation to 110 mg or 150 mg dabigatran twice daily or warfarin adjusted to an international normalized ratio of 2.0-3.0.

The drug was approved in 2008 in the European Union, Canada, and other countries for a shorter-term indication, primary prevention of venous thromboembolic events in adults after elective total hip or knee replacement surgery. Canada added the indication for stroke prevention in atrial fibrillation in October.

In the overall trial cohort, a stroke or systemic embolism occurred significantly more often in patients with a previous stroke or TIA (2.38% a year) than in those without such history (1.22%).

The primary outcome of stroke or systemic embolism occurred at similar rates between patients with a previous stroke or TIA who took warfarin (2.78% a year), 110 mg dabigatran (2.32%), and 150 mg dabigatran (2.07%). In the overall study population, the rate of stroke or systemic embolism did not differ among groups, occurring at 1.71% a year in patients on warfarin, 1.54% a year in patients on 110 mg dabigatran, and 1.11% a year in those on 150 mg dabigatran.

In the subgroup, intracranial bleeding occurred at a significantly lower rate in patients who took 110 mg dabigatran, compared with those who took warfarin (0.25% vs. 1.28% a year).

Patients with a history of stroke or TIA who took the 110-mg dose of dabigatran had a significantly lower rate of vascular death and all-cause mortality than did patients who received warfarin, but this effect was not seen in the 150-mg group. In this

subgroup, major bleeding also occurred at a significantly lower rate among only those who received 110 mg dabigatran.

The use of antiplatelet agents or nonsteroidal antiinflammatory drugs was balanced among the subgroups across the three treatment groups.

## Different Doses, Different Effects

Based on the results in patients with a previous stroke or TIA, the investigators suggested that "150 mg dabigatran might provide better protection against stroke than warfarin, whereas 110 mg dabigatran is as efficacious as warfarin and reduces adverse events (bleeding complications and mortality)."

And indeed, in the United States, the FDA's Cardiovascular and Renal Drugs Committee that evaluated dabigatran in September came to a similar conclusion, although no superiority claim over warfarin could be made. The FDA did not include the 110-mg dosage that established noninferiority in its approved dosages, recommending the regimen of 150 mg twice daily, except in patients with impaired renal function, who would take 75 mg twice daily.

How dabigatran might achieve a reduction in intracranial bleeding beyond a more stable anticoagulation "is not yet known," but Dr. Diener and his associates said that it might result from an inability to cross the blood-brain barrier.

**Disclosures:** Boehringer Ingelheim GmbH funded the study and markets dabigatran as Pradaxa. Dr. Diener and some of his authors disclosed financial relationships with this company and others that manufacture or market drugs for the prevention or treatment of stroke. One author is an employee of Boehringer Ingelheim. ■

COMMENTARY

**T**he advent of new anticoagulants that are easier to use is an important development. The risk of atrial fibrillation rises steeply with age, and the relative benefit of anticoagulants over antiplatelet therapy is greater in the elderly. Because warfarin has inter-individual differences, it requires dose adjustment and surveillance (*N. Engl. J. Med.* 2008;358:999-1008).

Physicians are reluctant to prescribe anticoagulation in the elderly because of concerns about dose adjustment, blood testing, confusion, compliance, and falls. It is crucial to understand that antiplatelet agents are effective only for white thrombus; and anticoagulants are necessary to prevent the formation of red thrombus. Under-anticoagulation in patients with atrial fibrillation, even those who with previous stroke or TIA, is a major problem (*Nat. Rev. Cardiol.* 2009;6:448-50).

This subgroup analysis of the RE-LY study confirms that the benefit of dabigatran shown in the main study persists in patients with previous TIA or stroke. It seems likely that in future we will be selecting doses of dabigatran based on renal function. Problems with dabigatran include interactions with drugs that affect P-glycoprotein, such as verapamil, amiodarone, and quinidine. Because grapefruit affects other transport proteins, this may be an issue.

J. DAVID SPENCE, M.D., is director of the Robarts Research Institute's Stroke Prevention & Atherosclerosis Research Centre and a professor at the University of Western Ontario (London). He is a researcher in the ARISTOTLE trial and has given lectures for Sanofi-Synthelabo and Boehringer Ingelheim.

## Temperature Also a Factor

Multiple Sclerosis • from page 1

In the study, 31 patients developed 310 new T2 lesions, whereas 13 patients had no new lesions. In 42 patients, imaging detected a mean of 22 new contrast-enhancing lesions per patient. Clinical attacks during this period were recorded on 51 occasions in 24 patients, with a mean of 2.1 per patient.

The distribution of disease activity across the seasons was distinctly higher in the spring and summer even after applying several different methods of correcting for individual disease severity.

The point estimates for the rate of new T2 lesion accrual per day were higher in the spring (0.024) and summer (0.030) than in the fall (0.010) or winter (0.016).

Disease activity also was strongly correlated with warmer

temperature and greater solar radiation, but not precipitation.

Patients with chronic, progressive MS tended to have an earlier and more pronounced high-activity period but lacked the peak of activity in August found in relapsing-remitting patients.

The findings did not change significantly in a separate analysis that excluded 18 patients who had been treated with brief bouts of steroids.

The findings could have an impact on MS clinical trials. The magnitude of an effect of the spring and summer on disease activity is likely affected by factors such as genetic affinity, disease phenotype, and geographic location, which "will have particular implications for multicenter trials that pool data from geographically distant

locations," according to the investigators.

They also noted that biases may arise in studies that use pre-screening MRI or in trials with crossover arms, depending on the timing of the trial arms.

**Disclosures.** Many of the investigators involved in this study disclosed that they had received research support from the National Institutes of Health and the National Multiple Sclerosis Society, as well as

research support, speaker honoraria, or served on scientific advisory boards from MS drug manufacturers, including Biogen Idec, Genentech, EMD Serono Inc., and Teva Pharmaceutical Industries Ltd. ■

COMMENTARY

**E**vidence for environmental factors in the pathogenesis of multiple sclerosis has accumulated ever since Dr. John F. Kurtzke's pioneering epidemiological work in the 1960s. Epstein-Barr virus infection, smoking, and vitamin D status have all been shown to exert effects on MS risk. There also have been reports of seasonal variations in disease activity measured as relapse rate and occurrence of optic neuritis, with higher incidence of both in spring and summer. Several studies have shown a correlation between month of birth and MS risk,

again with the highest risk in spring and summer.

Dr. Meier and colleagues report further evidence for a seasonal effect on disease activity and MS using serial MRI examinations. They elegantly show that disease activity, measured as new T2 lesions over time, varies over the year with a peak in spring and summer. They also show strong associations with solar radiation and daily temperature, but not precipitation. The levels of vitamin D in serum might be the causal link between season and disease activity, but this assumption

remains to be proven.

What is of great concern, however, is that MRI variables, a common measure of disease activity and thus treatment efficacy, seem to be influenced by season. This could bias trials aimed at assessing the effect of drugs on disease activity and need to be considered when designing future studies.

JONATAN SALZER, M.D., is a doctoral student in the department of pharmacology and clinical neuroscience at Umeå (Sweden) University. He has no relevant disclosures.



## BOOK REVIEW

# Handy Pocket Guide Puts the Facts at Your Fingertips

## Pocket Neurology

Edited by David M. Greer (Philadelphia: Lippincott Williams & Wilkins, 2010)

Many of us carried *Pocket Medicine* (The Massachusetts General Hospital Handbook of Internal Medicine) faithfully through intern year, finding solace in the middle of the night in its neat charts of abnormal electrolytes and causes of chest pain, and we can date ourselves by the color of the plastic binding on our edition. The shock of starting

At US\$45 on amazon.com, this 288-page guide will fit nicely in a white coat pocket, but is a bit heavier than *Pocket Medicine*. The formatting is user friendly, with good use of color and outlines making for easy scanning.

A text so thorough in its scope is unlikely to have many limitations, and in-

deed *Pocket Neurology* covers almost every base. The inclusion of references where evidence exists for clinical recommendations is essential, as it should be noted that some topics without references are possibly controversial, or might represent institution-specific guidelines. This is less of a limitation

than an important reminder for all neurologists that our guidelines are frequently changing and sometimes not entirely evidence based.

In summary, this is an impressively comprehensive pocket guide that is likely to prove useful to neurologists at all stages of practice. ■



BY SARAH MATTESON  
KRANICK, M.D.

Dr. Kranick is a clinical fellow at the National Institute of Neurological Disorders and Stroke at the National Institutes of Health, in Bethesda, Md., USA.

neurology residency was often accompanied by the realization that no similar ring-bound edition existed in our chosen specialty, leading many residents to devote hours to compiling charts and order sets into small, unofficial guides, usually specific to one's own program.

The residents and fellows of the Partners Neurology Residency Program in Boston have now produced a text truly worthy of being clutched by PGY-2s (second-year postgraduates) as they nervously begin their residencies, although this book will likely be useful to a much larger audience than junior residents alone. Designed to be "concise and complete," it impressively achieves both of these descriptors, although some may find it more complete than concise.

This text is impressive in its breadth and depth of information. In addition to the first section on "Neurologic Emergencies/Quick Reference," each subspecialty is covered in great detail, although at times, the level of detail seems beyond the scope of a pocket guide for residents, which instead makes the guide seem appropriate for neurologists at every level.

Junior residents may be overwhelmed by this level of detail and might have been aided by more clearly labeled tabs to reach the different sections more easily (neuro-oncology and neuro-ophthalmology, for example, are both labeled NO in the tabs) but they will likely find the thorough index very helpful in this regard.

The most clinically salient sections have large tables that make scanning these sections easier: the "Epilepsy" section has nice tables guiding the choice of antiepileptic drugs, and similarly helpful tables are found in every section. Overall, more illustrations, diagrams, or pictures would definitely add to the text and might be more helpful to some trainees rather than their carrying around a pocket guide that includes every epilepsy syndrome.



JOURNAL OF THE  
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Submission deadline March 31, 2011

## NEUROLOGY IN PRACTICE — PAKISTAN

## Global Links Help Build a Regional Specialty

I have practiced neurology in Pakistan for more than 25 years, during which time I have seen the field grow from a small, underresourced specialty into one with some excellent care and training centers and in which many more patients have access to treatments and diagnostic tools.

Take imaging, for example. We got our first CT scanner in Karachi in the early 1980s. It was a poor quality machine, but we at least had something. We also had to deal with inadequate maintenance backup, and not many people had been trained to use the machines, let alone interpret the scans. These days, CT scanning and MRI are cheaper and more accessible – we had 1 MRI machine in 1995 and now have about 36.



BY ARIF HEREKAR, M.D..

*Dr. Herekar is a consultant neurologist at Dow University of Health Sciences and medical director of the Neurodiagnostic Centre at Hamdard University Hospital, both in Karachi.*

### Care and Training

Pakistan is a developing country with only 50-60 fully qualified neurologists serving a population of 168 million, so almost every neurologist is both a child and adult neurologist – as well as a neuro-ophthalmologist, a physical rehabilitation specialist, and an epileptologist.

Institutions such as Dow University of Health Sciences and the Aga Khan University Hospital, both in Karachi, have steadily improved the quality of care and created better diagnostic facilities. But not all patients have access to such high-end care. General hospitals, which cater to the majority of patients, have neurological facilities but they are limited.

Quality and scope of training have improved. There are more postgraduate facilities, and we hope that as neurology expands as a specialty, these fields will produce their own experts. There are postgraduate institutions such as the College of Physicians & Surgeons Pakistan, whose qualification is recognized internationally.

### Focus on the Clinical Examination

In the absence of diagnostic tools and reliable, applicable research data, neurologists have learned to rely heavily on the clinical examination, focusing on the signs and symptoms the patient presented with. This has produced some outstanding clinicians. Such examinations can be long and tedious and often inconclusive because the diagnoses depend on the experience of the

neurologist – his or her experience essentially defines the quality of examination.

Lumbar puncture was – and is – widely used. Every young doctor learns the procedure. Although it is risky to do without a CT scan or MRI, it is still common because tuberculous meningitis, which remains prevalent in Pakistan, cannot be diagnosed and treated without CSF cytology and biochemistry.

Subacute sclerosing panencephalitis cases related to the measles infection are also more prevalent in Pakistan, compared with in developed countries with routine immunization programs, as are the various CNS manifestations of tuberculosis and tuberculomas. More generally, in our daily practice we treat headache; epilepsy (see box); stroke; Parkinson's disease; childhood disorders such as headache, mental retardation, leukodystrophies, and poliomyelitis (though much less now); and other progressive neurological disorders.

Dr. Herekar is a consultant neurologist at Dow University of Health Sciences and medical director of the Neurodiagnostic Centre at Hamdard University Hospital, both in Karachi.

### Drugs and Herbal Remedies

The specialty has benefited from the enormous advances in drug and treatment options. One small example: From the first-line antiepileptic drugs such as phenobarbitones, phenytoin, and carbamazepine, we can now use drugs such as topiramate and lamotrigine more frequently. With a greater variety of second-line antiepileptic drugs, fewer children are exposed to high doses of phenobarbitone, which is particularly important given the drug's adverse effects, such as hyperactivity and scholastic decline.

Herbal and alternative medical options are used more frequently in Pakistan than elsewhere, especially in remote areas. Some centers where herbal remedies have been used have reported improvement in children with mental retardation, but there have been no authenticated studies to date. Patients in remote rural areas also tend to rely more heavily on spiritual treatment through traditional healers, though again, no data are available on the effectiveness of these options.

### Advances in Research and Surgery

Neurophysiology research also has come a long way in the last 2 decades. We now have EEG monitoring and

sleep studies being conducted at a number of centers. Some researchers have begun exploring stem-cell therapy with limited success, but they are persevering.

Surgery for epilepsy is starting to be used more widely, as is stereotactic thalamotomy. And even though Pakistan is a poor country, we have a gamma knife radio surgery facility available. The procedure has been used mostly for metastatic tumors, meningiomas, arteriovenous malformations, acoustic neuromas, gliomas, and some pituitary adenomas. Many people in developing countries are jittery about surgery and are more comfortable with nonsurgical procedures, so gamma knife surgeries are used frequently.

It follows from the many advances in care, treatment, training, research, and surgery that rehabilitation services have also improved over the years. Having rehabilitation centers and occupational and speech therapy centers for handicapped and debilitated children means that outcomes in general are improving.

### Connectivity Is the Key

Much of this progress has been made possible by neurologists in Pakistan being able to link up with the global neurological community through the Internet by participating in online exchanges and teleconferences. The Web also allows for easier and quicker access to research findings and clinical andv therapeutic advances. ■

## Epilepsy Facts and Fiction

Despite advances in neurology in Pakistan, there are regions where medical resources and access to them remain limited. Because of this, there are not much data on most neurological diseases. Here are some data on epilepsy:

- ▶ There are about 2 million people with epilepsy in Pakistan;
- ▶ One survey found that 28% of people with epilepsy in more developed areas of the country seek and get medical help, compared with 1%-2% in rural areas;
- ▶ The disease is 1.5 times more prevalent in women than in men;
- ▶ Another survey found that 20% of respondents in a rural area thought that people with epilepsy should never marry; and
- ▶ 7%-10% thought it was a contagious disease.

## Applications Double for European Board Examination

BY SVEIN MELLGREN, M.D.,  
PH.D., AND  
WOLFGANG GRISOLD, M.D.

The number of successful candidates at the second European Board Examination in Neurology doubled to 12 from last year's 6. All other numbers – for applications, eligibility, and those who sat for the examinations – were also notably higher than last year's.

Of 39 applicants (12 last year), 25 were eligible for the examination (7 last year), and 16 sat for it (6 last year). The 12 candidates who passed are now recognized as fellows of the Union Européenne des Médecins Spécialistes (UEMS) and the European Board of Neurology (EBN). Unsuccessful candi-

dates will be able to take the examination again when next it is offered.

The examination took place during the European Federation of Neurological Societies (EFNS) congress in Geneva in September. It was developed by the EBN, a division of the Brussels-based UEMS, in collaboration with the European Neurological Society (ENS) and the EFNS.

The UEMS represents the national associations of medical specialists in the European Union. Several medical specialties, but not neurology, have had board examinations in place for a number of years. But that changed last year for neurology when, after a 3-year developmental stage, the EBN launched its European board examination at the ENS congress in Milan.

The examination has been designed for UEMS member states in which training and skills are approved by the national medical societies. This year, Turkish candidates were also admitted to sit for the examination.

An applicant must have been admitted to his or her national medical society to guarantee practical training and assessment in the specialty. Those who are deemed eligible have to complete a 120-item multiple-choice test and a structured oral presentation focusing on four cases. They can also elect to do a short presentation on a separate case or research work for extra credit.

The questions are devised by the scientific panels of the ENS, EFNS, as well as members of the UEMS and EBN,

then entered into a database for independent evaluation by the examination committee. Questions above the passing limit are evaluated by medical education experts at Ege University, Izmir, Turkey, for accuracy and clarity.

The next examination will take place next year on May 27 at the ENS congress in Lisbon.

For more information, please visit [www.uems-neuroboard.org](http://www.uems-neuroboard.org). ■

PROF. MELLGREN is in the department of neurology at the University Hospital of North Norway in Tromsø. He is vice president of the UEMS and EBN and chairs the education committee. PROF. GRISOLD is the past president of the UEMS and EBN and a WFN Elected Trustee.



# Vitamin E Trial Hints at Improved Brain Injury Outcomes

BY LAIRD HARRISON  
Elsevier Global Medical News

High doses of vitamin E significantly decreased in-hospital mortality following a traumatic brain injury in the first-ever randomized, controlled clinical trial of this treatment.

High doses of the vitamin cut in-hospital mortality from traumatic brain injury (TBI) by 29% relative to the overall mortality of patients who received treatment with low or high doses of vitamin C or placebo. The study also showed the benefits of high-dose vitamin C in stabilizing or reducing the diameter of perilesional edema and infarct, said Dr. Ali Razmkon, a neurosurgery resident at the Shiraz (Iran) University of Medical Sciences, at annual meeting of the Congress of Neurological Surgeons in San Francisco.

The theory behind the study is that lipid peroxidation causes secondary damage in head injuries. "There are well-documented

of follow-up than any of the other groups.

Diameters of the perilesional hypodense regions in the brains of patients taking high-dose vitamin C were stabilized or reduced over the course of 7 days, dropping from a peak mean diameter of 12 mm on the third day after admission to 8 mm on the seventh day. This was significantly different from what was seen in patients in the other groups, which all had perilesional edema that continued to increase in diameter. The researchers con-

cluded that low-dose vitamin C didn't affect the patients' healing but that high doses slowed the progression of perilesional edema, likely a result of secondary oxidative insults. Neither dose seemed to affect neurologic outcomes.

In an interview, Fernando Gomez-Pinilla, Ph.D., of the University of California Los Angeles, said vitamin E has shown promise in protecting the brain against the effects of TBI. "Its powerful antioxidant action seems effective in reducing free

radical contents in the brain, which would otherwise impede optimal function of neurons. The vitamin has also shown positive effects on reducing memory decay and is a strong candidate for reducing cognitive impairment in Alzheimer's disease," said Dr. Gomez-Pinilla, professor of neurosurgery, and integrative biology and physiology at UCLA.

The Iranian National Elite Foundation funded the study. The researchers and Dr. Gomez-Pinilla reported no conflicts. ■

## IN PATIENTS ON HIGH-DOSE VITAMIN C, THE DIAMETERS OF THE PERILESIONAL HYPODENSE REGIONS WERE STABILIZED OR REDUCED OVER 7 DAYS.

reports about vitamin C in human stress in many conditions, including common cold and stroke," Dr. Razmkon said in an interview. "Plasma concentration is reduced. The body needs more and uses more."

Previous studies have suggested vitamin C could reduce the risk of stroke and that vitamin E could decrease the rate of lipid peroxidation.

To test this theory, Dr. Razmkon and his colleagues at Shiraz enrolled 100 patients (83 men) with traumatic brain injury. The patients all had Glasgow Coma Scale scores of 8 or less and radiologic diagnoses of diffuse axonal injury. Patients with significant liver or renal disease, previous head injury, or glucose-6-phosphate dehydrogenase deficiency were excluded.

They randomly assigned patients to low-dose intravenous vitamin C (500 mg daily) for 7 days, high-dose intravenous vitamin C (10 g on admission and again on the fourth day, then 4 g daily for 3 more days), intramuscular vitamin E (400 IU daily) for 7 days, or placebo. The groups had no significant differences in diagnosis, age, or sex.

During the study, 26 patients died, and 67 (91%) of the remaining 74 patients attended follow-up at 2 and 6 months.

Hospital mortality was significantly lower in patients in the vitamin E group (20%) than in the groups receiving low- or high-dose vitamin C (30% and 29%) or placebo (33%). In-hospital mortality was 28% overall in these other three groups. At 6 months of follow-up, no differences in mortality were seen between the vitamin E (30%), low- and high-dose vitamin C (35% and 29%), and placebo groups (33%).

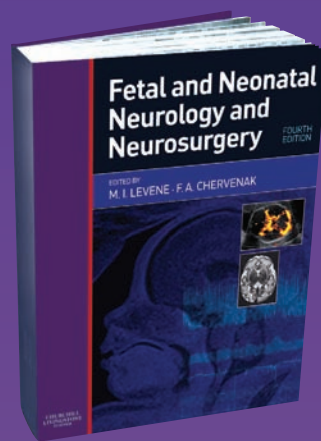
The vitamin E group also had significantly better Glasgow Outcome Scale scores at discharge and at 2 and 6 months



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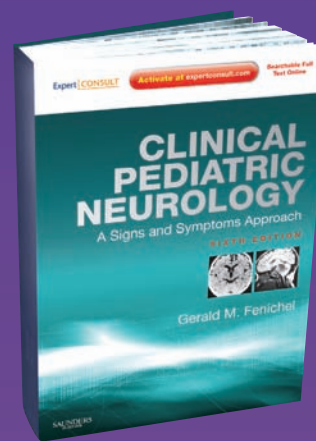
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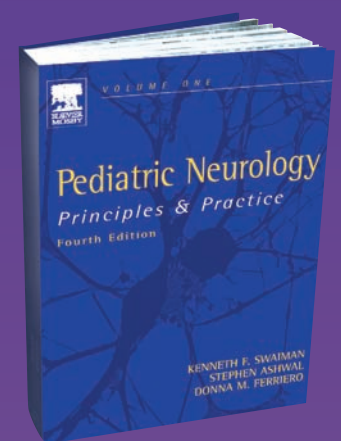
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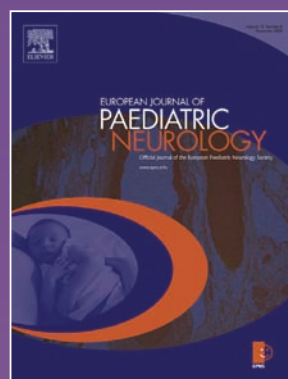
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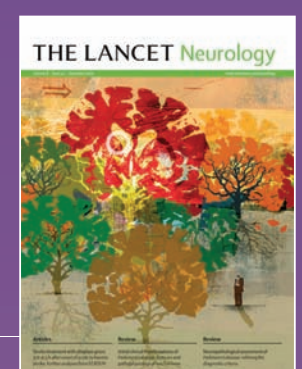


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## FROM THE JOURNAL OF THE NEUROLOGICAL SCIENCES

# Silent Cerebral Aneurysms More Common in Women

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

Stroke patients have generalized vascular disease, often involving vessels of various types in various organs. Thus, strokes, myocardial infarctions, retinopathy, nephropathy, and large and small peripheral vessel disease all have common risk factors and tend to appear together in an affected individual. Furthermore, their risk factors are also risk factors for other vascular diseases such as aneurysm, and possibly for putatively nonvascular conditions such as Alzheimer's disease.

The coincidence of these diseases involving different sets of vessels is most likely not by chance, and it is reasonable to ask whether some combinations of them are more likely than others. Do microvascular diseases occur more commonly together, so that leukoaraiosis is seen more often with small vessel disease of the heart (with recurrent congestive failure) than with stenosis of the iliac artery (with intermittent claudication)? Or is carotid stenosis more likely to occur in a patient with coronary artery stenosis than in a patient with diffuse nephropathy? Similarly, do aneurysms occur more commonly in brain hemorrhage than in infarct?

A particularly interesting and clinically relevant question for the vascular neurologist focuses on the significance of asymptomatic cerebral aneurysms (CA) that are discovered in patients who have had strokes. Is there

a higher risk of CA in particular stroke subtypes? Does the presence of CA in stroke patients imply a worse outcome than in stroke patients without CA?

Dr. Yuichi Ishikawa and his colleagues in the department of neurology at Toho University's Omori Medical Center in Tokyo examined these questions in a series of 492 stroke patients who were seen at the center during 2007-2008. They evaluated the patients for CA by magnetic resonance angiography (MRA) and compared its prevalence in brain infarction and brain hemorrhage patients and controls. The researchers found that 3.5% of the brain infarct group, 4.7% of the brain hemorrhage group, and 2.1% of controls had CA. There was no significant difference among the groups in prevalence, size of aneurysm, and its location. There were no ruptures in any of the aneurysms 3 months after the MRAs were done.

However, the risk of having CA was greater in women than in men with stroke ( $P$  less than .01); the risk of CA was also greater in women than it was in men in the control group ( $P$  less than .01; *J. Neurol. Sci.* 2010;298:42-5).

The prevalences were somewhat higher than in other studies, possibly because different detection methods

were used or the study population differed from those in previous studies or both. It would be interesting to see data from studies using the same detection methods in other population groups. The value of the study lies in the suggestion that aneurysms may be in part a coincidental epiphenomenon, appearing equally in different stroke types and in normal controls, and can be considered as a separate issue.

Dr. Ken Ikeda, the senior author of this study, has long had an interest in the study of stroke prevention and treatment. He notes that although the presence of cerebral aneurysms in stroke patients is uncommon, it can make the assessment and management of the patient more challenging. However, this does not tell us that the use of anticoagulants and TPA is beneficial or even safe in such patients, and physicians should "examine incidental CA cautiously in female BI patients" who are treated with TPA. Dr. Ikeda and his colleagues asserted in their report. The researchers are planning studies to address these issues. ■

DR. TSELIS is associate professor of neurology at Wayne State University in Detroit, USA, and book review editor for the *Journal of the Neurological Sciences*.

**RISK FOR CEREBRAL ANEURYSM WAS GREATER IN WOMEN THAN IT WAS IN MEN WITH STROKE AND MALE CONTROLS (BOTH  $P$  LESS THAN .01).**

## Palatucci Fellows Pass On Leadership, Advocacy Message

Graduates of the American Academy of Neurology's Donald M. Palatucci Advocacy Leadership Forum have established a working group within the World Federation of Neurology to teach the forum's advocacy techniques at an international level.

The purpose of the program is to train neurologists in effective advocacy for patients, caregivers, and the public at the local, state, and national levels. About 240 neurologists have trained through the leadership forum since its launch in 2003. Fellows have come from Australia, Austria, Belgium, Canada, China, Jamaica, Japan, Georgia, Guatemala, India, Ireland, Nigeria, Pakistan, the Philippines, Sri Lanka, and the United States.

Now, two Palatucci fellows, Dr. Man Mohan Mehndiratta, professor of neurology at the G.B. Pant Hospital, Delhi University, India, and Dr. Mohammad Wasay, associate professor of neurology at Aga Khan University, Karachi, Pakistan, are leading the effort to train other neurologists in the techniques and tools of advocacy they learned during their participation in the forum. So far, they have conducted advocacy skills development programs in Australia, India, the Philippines, Sri Lanka, and Thailand, together with Dr. Michael Finkel.

The first international program was presented in New Delhi in 2008. The faculty included Palatucci fellows from India, Pakistan, the Philippines, and the United States, with onsite support from AAN advocacy staff and the local organizers of the 12th Asian Oceanian Congress of Neurology and the 16th annual



Faculty members and organizers at an advocacy workshop held in India: They are (back row, from left), Dr. Lakshmi Ranganathan, Dr. Tarakad Ramachandran, Dr. Michael Finkel, Melissa Larson; and (front row from left) Amy Kaloides, Dr. Mohammad Wasay, Dr. Apoorva Pauranik, and Dr. Man Mohan Mehndiratta.

conference of the Indian Academy of Neurology. Four of the new fellows helped form an advocacy subsection of the Indian Academy of Neurology.

Also in 2008, the team trained 12 advocates at a workshop on advocacy in stroke care during the 5th Asia Pacific Conference Against Stroke in Manila, the Philippines. Among the other workshops was one in Colombo, Sri Lanka, during the 2nd Annual Scientific Meeting of the Association of Sri Lankan Neurologists; and another at the 6th Asia Pacific Conference Against Stroke in Cairns, Australia. And at last year's World Congress of Neurology in Bangkok, finally, about 40 neurologists from numerous countries enrolled in a full-day advocacy workshop. The program offers workshops in:

► **Action planning.** Participants learn to plan, identify goals, and focus on timeliness.

► **Media training.** They are coached in giving interviews to raise awareness of the program.

► **Grassroots legislative training.** Fellows learn the importance of understanding how government works to help them achieve desired legislative outcomes.

Results of the advocacy training can be rapid and concrete. After Dr. Wasay went through the training program, he returned to Pakistan to head the tetanus and rabies eradication task force of the Pakistan Society of Medicine, in collaboration with the Infectious Disease Society of Pakistan and the country's ministry of health. The group carried out a survey

about public awareness of these disorders, and a new tetanus and rabies eradication program is now active in Karachi (*J. Pak. Med. Assoc.* 2008;58:157-8).

The advocacy team plans to hold more training workshops in other Asian countries and to expand to Africa. The cost of the programs has been modest, with faculty and AAN staff contributing their time and expertise.

Two other initiatives are under discussion: the establishment of global days of recognition to focus attention on certain neurological disorders; and starting an online advocacy resource center from which WFN member societies and individuals can obtain guidance and materials.

The Donald M. Palatucci Advocacy Leadership Forum honors the memory of Donald M. Palatucci, M.D., who was a member of the American Academy of Neurologists' board of directors. It is funded by the fellowship established in his name, and organized by the AAN.

For more information about the program, e-mail Dr. Mehndiratta (mmehndi@hotmail.com), Dr. Wasay (mohammad.wasay@aku.edu), or Melissa Larson (mlarson@aan.com); or go to [www.aan.com/go/advocacy/active/palf](http://www.aan.com/go/advocacy/active/palf). ■

By Man Mohan Mehndiratta, M.D., Chair, WFN Task Force on Advocacy; Mohammad Wasay, M.D., Chair, WFN Public Awareness and Action Committee; Michael Finkel, M.D., President, World Foundation of Neurology; and Donna Bergen, M.D., Chair, WFN Applied Research and WHO Liaison committees.



## WFN NEW MEMBER – KAZAKHSTAN

## Quality Training and Care Top the Agenda

BY ALTYNAY KARIMOVA, M.D.

The League of Neurologists of Kazakhstan was established in November 2008 by a group of 12 neurologists. Dr. Nurlan Kaishibayev of Kazakh National Medical University, Almaty, and chief neurologist at the Kazakhstan ministry of health care, is chair of the league. The general secretary is Dr. Gulnaz Kaishibayeva, deputy director of the Institute of Neurology in Almaty, and Dr. Leila Dairbayeva, also of the Institute of Neurology, is the treasurer. League membership now stands at 50.

**Mission and Activities**

The league's mission is to care for neurological health by working to ensure access to high-quality care that is delivered ethically; facilitate training for neurologists, primary care physicians, and other providers; support research; and disseminate neurological information.

A significant amount of time and resources is dedicated to education and training, especially at the postgraduate level. We are careful to ensure that the training and technology are in line with global standards and are working on introducing a continuous medical education program and providing supplemental training for health care workers and patients and their relatives.

We also place great value in connecting with our regional and international colleagues by participating in congresses, meetings, and symposiums, and by collaborating in research. We maintain close contact with our neurology col-



**Dr. Altynay Karimova says neurological data are being gathered for registries.**

leagues in neighboring Uzbekistan, Kirgizstan, and Russia and have formed an alliance with the European Federation of Neurological Societies.

**Putting Registries to Good Use**

About 500 out of every 100,000 people in Kazakhstan die annually from cardiovascular diseases and about half those deaths are caused by stroke. According to data from a stroke registry that has been in place since 2005, a total of 15,000 people have suffered strokes in the last 4 years, and about 40% of those patients died.

Unfortunately, there are no official data for any other neurological conditions. However, since May, we have had registries on epilepsy and transient ischemic attacks and we hope soon to be



**Dr. Gulnaz Kaishibayeva is the general secretary of the Kazakhstan league.**

able to analyze the data on these two conditions to help inform government and health policy makers in the hope that the infrastructure for diagnosing, treating, and managing neurological diseases can be improved. We have similar registry plans for neurorehabilitation, demyelinating diseases, and myasthenia.

**Primary Care and Practice Facilities**

In Kazakhstan, a succession of specialists might cooperate in treating a patient. The patient will first consult with a primary care physician, who might refer to a specialist, as is usual for patients using government-run practice facilities. Some patients might consult directly with a neurologist, but that is usually the case for patients who can afford a private clinic.

Governmental care is well developed and free for children and mostly free for adults, who have to pay for some services. The average price for an examination in a private hospital is 3,000 tenge (US\$20). The services are available at polyclinics, emergency care, and hospitals as well as at specialized medical institutions such as the Institute of Neurology in Almaty and Institute of Neurosurgery in Astana. More people are starting to use the private clinics because of the shorter waiting times.

**Training and Salaries**

Neurologists can train in Kazakhstan at nine higher medical institutions. The country has 1,506 neurologists – 10 per 100,000 of 15,219,300 people.

Trainees pay for their own postgraduate specialty training, starting at a monthly rate of 55,000 tenge (about US\$380). If there is a shortage in a particular specialty in one of the regions, then the regional administration will fund a candidate's postgraduate training in that specialty. Qualified neurologists earn very low salaries – the average range is US\$200-400 monthly.

Specialists have few resources to cover the costs of improving their skills. Many rely on self-study in libraries or on the Internet, but that too, is limited, because most regions do not have medical libraries or Internet. That is why we channel so much of our resources into quality postgraduate training for neurologists. ■

DR. KARIMOVA is the coordinator at the League of Neurologists of Kazakhstan.

## Stroke Straddles Four Decades of Medical Progress

Over the course of its 40 years, the journal *Stroke* has gone from strength to strength, and as is often the case with specialty publications, it has mirrored the remarkable advances in the field it is dedicated to covering – stroke and cerebral vascular diseases.

In 1970, the year of its launch with Clark Millikan as the first editor-in-chief, there were no therapies for treating or preventing stroke, hypertension was the only established a risk factor for stroke, and imaging of today's sophistication would have been difficult to conceive of (*Stroke* 2010;41:1073-5). In fact, the journal, which is published by the American Heart Association, was started in response to a growing interest in stroke – both clinically and as fertile ground for scientific research work, according to Fletcher H. McDowell, who edited the journal from 1977 to 1981 (*Stroke* 2001;32:595-6).

A number of pivotal stroke studies were published in the early 1970s. The Canadian Aspirin Trial, for example, led by Henry J.M. Barnett (editor-in-chief, 1982-1987), found that antiplatelet drugs could prevent stroke. Such findings triggered other investigations: Additional risks, including smoking and lipidemia, were identified, paving the way to more effective prevention measures; enhanced neuroimaging tools revolutionized stroke diagnosis; and preventative and restorative therapies in the form of statins and platelet antiaggregants were refined as were surgical interventions such as endarterectomy and stenting. More recently, investigators

have begun exploring the role of genetics in stroke and examining systems of care and rehabilitation.

*Stroke* has delivered many of these groundbreaking studies to the neurological community, making it a trusted and sought-after source for clinical and scientific developments. That standing is reflected in numerous ways. For example, annual submissions have risen steadily over the journal's lifetime, with this year's number fast approaching 3,000, which could possibly double the 2000 figure of 1,476. They doubled during the previous decade as well, from 563 in 1991 to 1,476, according to Mark L. Dyken, the editor-in-chief from 1992 to 2000 (*Stroke* 2001;32:2730-3). The only dip in submissions was in 1990, when two new stroke journals were launched. As submissions from the United States and overseas increased, so too did the number of pages and articles per issue. Little surprise then, that in 1988, the journal switched from publishing bimonthly to monthly while under the editorship of Oscar M. Reinmuth (1987-1991; *Stroke* 2010;32:2211-2).

Another area of steady growth has been in subscriptions – more so since the journal went online and also since it began publishing foreign language editions in 2002. *Stroke* is now available in Spanish, Russian, Italian,

Japanese, Chinese, Portuguese, Korean, and Turkish, and the English edition is available in India. The availability of foreign language editions were a fulfillment of one of the priorities set by Vladimir Hachinski, currently President of the World Federation of Neurology, at the beginning of his tenure as the journal's editor-in-chief (2001-2010; *Stroke* 2010;41:833-5).

*Stroke's* success could be summed up by its impact factor, which denotes the frequency with which a journal's articles are cited.

In 2002, *Stroke's* impact factor was 5.176 and it is currently 7.041, almost twice that of its nearest competitor.

This year, Mark Fisher of the department of neurology at the University of Massachusetts takes over the 5-year editorship from Dr. Hachinski. Among his priorities are to continue to foster growth and innovation within the journal, to expand its scope internationally, and enhance online data supplements. Yet, he cautions, "many challenges must be confronted. The traditional model of medical publishing is under siege ... and the financial viability of the enterprise is being severely tested" (*Stroke* 2010;41:1312-3). ■

This article is based on material provided by *Stroke*.



DR. FISHER

**'The traditional model of medical publishing is under siege,' and financial viability is being tested.**



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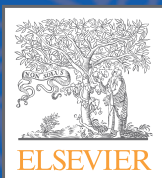
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## NEUROLOGICAL HISTORY

## Student, Mentor, and Lifelong Friends and Colleagues

*I became his most devoted disciple, reading everything he wrote, and ready at any time to listen to his pithy conversation and wise aphorisms.*

—HENRY HEAD, of the German physiologist, Ewald Hering

In the late 19th and early 20th centuries, many neurologists forged professional relationships with their overseas counterparts. With that exchange of clinical and scientific knowledge often came cultural exchange and lasting friendships, as was the case with the German physiologist, Ewald Hering (1834-1918) and the English neurologist, Henry Head (1861-1940).

Before Head matriculated at Trinity College in Cambridge, England, to read for the Natural Sciences Tripos, he worked in Germany with the physiologist Julius Bernstein. Back in England, he completed the Tripos with a first class honors, then returned to the continent, this time to Prague, where he studied for 2 years under Hering at the German University, where Hering had become professor of physiology at the age of 36 in 1870. Head later wrote of his first meeting with Hering: "I found him at work and was instantly impressed both by his genial personality and by the splendid opportunities for research displayed in his laboratory."

Hering's research on binocular vision contributed substantially to the study of strabismus. In his ingenious work on eye movements – he placed a small "stethoscope" against the eyelids to "listen" to eye movements during reading – he reported hearing clapping sounds that he related to the displacement of afterimages, alternated with pauses when the reader was asked to fixate a stationary target.

He was one of the first investigators to observe what is now recognized as saccades – outside of the context

of vestibulo-ocular reflexes. And he discovered that apparently smooth eye movements during reading in fact consist of jerky movements of the eyes.

In later years, Hering also studied the respiratory reflexes in cooperation with Joseph Breuer, an Austrian physician whose early work paved the way for psychoanalysis. Their collaboration remains well known today, encapsulated in the eponym "Hering-Breuer reflexes," which describes the vagus nerve-mediated reflexes that control expiration and inspiration.

Hering returned to that subject when the 23-year-old

Head arrived in Prague. Head subsequently repeated Breuer's respiration experiments, although by then he was able to apply improved methods that allowed him to make accurate recordings (kymographs).

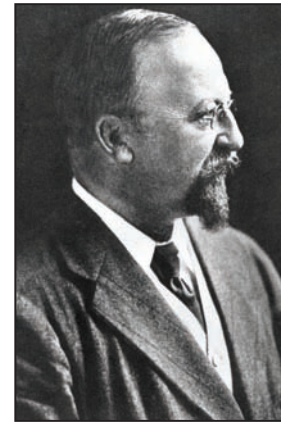
After Head returned to England he became a clinical neurologist, but the lessons from his time with Hering in Prague probably influenced his study of the physiology of human sensation and in particular, the importance of psychological investigation in physiological research.

He studied the pain of visceral disease, which was the subject of his thesis for his

medical doctorate in 1892 (J. R. Soc. Med. 1991;84:107-9). According to Caoimhghín S. Breathnach, author of the 1991 article, Head asserted that "tenderness in consistent cutaneous areas found in visceral disease bore some definite relation to nerve distribution." Those patches of hyperalgesia are known today as Head's areas. He later published, with Alfred Walter Campbell, on the pathology of herpes zoster and its bearing on sensory location (Brain 1900;23:353-524). Such was Head's desire to understand and explore that he had cutaneous branches of his arm transected and sutured in a study of the sensory effects of nerve healing, which he undertook with William Rivers, the English anthropologist and psychologist.



BY PETER J. KOEHLER, M.D., PH.D.



Henry Head, left, studied the physiology of sensation; Ewald Hering, right, investigated eye movements.

Head's work on aphasia was inspired by the writings of John Hughlings Jackson, known as "the father of English neurology" and a pioneer in research in epilepsy, aphasia, and neuro-ophthalmology. In his correspondence with the Swiss neurologist, Constantin von Monakow, Head admitted how difficult the papers were, "even for an Englishman." Nevertheless, his studies on the subject culminated in the two-volume work, *Aphasia and Kindred Disorders of Speech* (New York: Macmillan Co., 1926).

A recent biography on Head also highlights his literary prowess as a poet and writer, a talent that had been kindled during his time in Germany and one that he shared with his wife, Ruth, a novelist. She had edited compilations of the works of Thomas Hardy (for which Head had written the introduction) and Henry James.

The biography charts Head's struggle with Parkinson's disease, which forced him into early retirement (*Medicine and Modernism: A Biography of Sir Henry Head*, by L.S. Jacyna. London: Pickering & Chatto).

For more information on the relationship between Hering and Head, see *J. Hist. Neurosci.* 2005;14:322-33.

## WFN TRAVELLING FELLOW

## Hands-On Workshops Help Refine Practical Skills

BY GAYAN AGHAKHANYAN, M.D.

The World Federation of Neurology's travelling fellowships offer neurologists from low- and lower-middle income countries the opportunity to attend neurological meetings where they can broaden and strengthen their clinical and scientific knowledge, meet colleagues from other countries, and learn about the latest innovations and technology.

Through the fellowship, I attended the 14th congress of the European Federation of Neurological Societies in Geneva in September. The scientific program featured lectures on clinical neurology and clinical and basic neuroscience. There were also teaching courses (some of which were free and greatly appreciated), hands-on courses on clinical neurophysiology, workshops, and satellite symposiums.

I was inspired by the lecturers' expertise and the depth of their presentations. I es-

pecially enjoyed a lecture on Parkinson's disease and movement disorders, and another on behavioral neurology. I came away with new insights into the clinical application of deep brain stimulation and aspects of cognitive neuroscience and the neuronal basis of behavior.

Two symposiums on epilepsy were extremely useful and informative. One addressed drug-resistant epilepsy, and the other, presented by the EFNS and EUREPA (European Epilepsy Academy), dealt with treatments in general. EUREPA and the International League Against Epilepsy collaborate on a distant education program called VIREPA (Virtual Epilepsy Academy of the European Epilepsy Academy and the EUREPA), in which I have participated to update and refresh my epileptological knowledge.

I presented a poster based on work I had done with my colleagues, Henry Bakunts, Alexei C. Torosyan, and Kristina F. Bagdasaryan, entitled, "Products of the Catabolic Breakdown of Cell Recep-



Dr. Gayan Aghakhanyan also presented a poster on R-protein breakdown.

tors (R-Proteins) in Patients With Cerebrovascular Disorders." I also represented Armenia on Prof. Bakunts' behalf at the annual general meeting of the WFN

Council of Delegates. It was fascinating to see the officers, committee chairs, and delegates, headed by the President Vladimir Hachinski, working together on Federation business. I am now eager to be more involved in neurological society activities in Armenia, because I can see that by doing so we can raise our standards of neurological care.

Learning is a continuous task for all clinicians and scientists. Being at the congress helped me refine my practical standards and improve my knowledge of neurological disorders, patient care, and research techniques. I think that now I have a deeper understanding and appreciation of neurology and neuroscience.

I would like to express my gratitude to the WFN for offering the fellowship and I thank it for this opportunity.

DR. AGHAKHANYAN is in the department of angioneurology at the National Institute of Health and in the European Medical Centre – Stroke, in Yerevan, Armenia.



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## Reports Reflect Vibrant Agenda

Council of Delegates • from page 1

tenure, continues to support it with Prof. Njamnshi.

Trustee Ryuji Kaji (Japan) described the Asia Initiative, which Jun Kimura (Japan), another Past-President, supports. Again, Dr. Kaji emphasized education, including a program on traveling fellowships. Dr. Hachinski noted that the Asian region has more than half of the world's population.

Another Trustee, Gustavo Roman (USA), described the Latin America initiative that has support from Albert Aguayo (Canada). This program will help support the Pan American Congress of Neurology in La Paz, Bolivia (March 5-8, 2012). Dr. Roman said the initiative is contributing to the development of a new residency program in Panama, similar to that developed in Honduras by Marco T. Medina with WFN help.

### Committee Updates and New Members

William Carroll (Australia), chair of the Membership Committee, described several activities of his committee. One is to reevaluate the WFN's dues and voting structure. Countries vary widely in their numbers of members (and the amount they pay in dues), but each currently has the same one vote. A second task is to try to increase the number of member countries, which of course might entail the development of neurology as a specialty in countries where the field is poorly developed.

Dr. Bergen, chair of the Applied Research Committee, noted that there are currently 27 Applied Research Groups, which vary widely in their activities and some of which are very strong and active. She is trying to improve communications between the groups and the WFN and offered help where needed.

The next item on the agenda was voting on three new member societies. Their applications had been passed already by the Membership Committee and the Trustees, but each society needed separate action by the Council of Delegates. The societies were Ivory Coast (its representative, Therese Sonan, was not able to attend); Palestine, which was represented by Adel Misk; and Yemen, represented by Hesham Awn. All three societies were elected unanimously.

It was of note that the motion to admit Palestine was made by Natan Bornstein from Israel and seconded by Dr. Freedman. Dr. Hachinski made a special mention of this, reminding the delegates again of the cooperation of China and Taiwan seen earlier in the meeting.

### Marrakesh Congress Plans on Track

El Mostafa El Alaoui Faris (Morocco), the President of the upcoming World Congress in Marrakesh, noted that the plans for the Congress are going very well and many of the scientific sessions are already organized. He extended an



Alfred K. Njamnshi (Cameroon) gave a presentation on the Africa Initiative.



William Carroll (Australia), Membership Chair.



Ahmed Khalifa (Syria), Pan Arab Regional Director.



WCN President, El Mostafa El Alaoui Faris (Morocco).



The Secretary-Treasurer General, Raad Shakir.



Riadh Gouider (Tunisia), left, and Morris Freedman (Canada), right, the Co-chairs of the Education Committee's e-learning task force.



Donna Bergen and Stephen Sergay, both from the United States, were appointed as co-opted trustees.

invitation for all to attend. In response to a question about travel to Marrakesh, he said that there are several flights directly to Marrakesh, but if travelers were to come to the busier airport in Casablanca, bus transportation to the Congress venue would be arranged.

Dr. Hacke reported on the Congress Organizing Committee's plans for the 2015 Congress, which is to be held in the Americas. A few countries have already submitted their bids to host it, and the organizing committee will evaluate the bids and put forward a slate of the top applicants to be voted on at the Marrakesh meeting.



Asian delegates, from left, Shigeki Kuzuhara (Japan); Ching-Piao Tsai (Taiwan), Regional Director for Asia-Oceania; Trustee Ryuji Kaji (Japan); and Beom S. Jeon (Korea).



From left, WFN Officers, Vladimir Hachinski, Raad Shakir, and Werner Hacke, with Elected Trustees, Gustavo Roman, Wolfgang Grisold, and Ryuji Kuji.

Dr. Hacke also noted that the plans for the 2013 meeting in Vienna were moving along well.

Dr. Kaji had served to the end of his first term as an Elected Trustee. He was eligible to run for a second term, and since no candidate came forward in opposition to him, he was reelected by acclamation.

Two new Regional Directors were introduced at the meeting. Ahmed Khalifa (Syria) was introduced as the new Regional Director for the Pan Arab region. He noted an upcoming congress in Bahrain and spoke about efforts in the region to improve the quality of pa-

tient care and increase emphasis on subspecialty development. Prof. Tsai was introduced as the new Regional Director for Asia-Oceania.

The Secretary-Treasurer General, Raad Shakir, delivered the financial report. He made clear that the organization was doing well, with capital of £2,643,334, including a reserve of £1,400,000.

Dr. Shakir noted that the accounts have been audited and asked for – and received – approval to reappoint the auditors. Dr. Shakir mentioned that small amounts of funds were available to seed new projects, and he welcomed applications.



# XX<sup>th</sup> WORLD CONGRESS OF NEUROLOGY

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