VOL. 24 • NO. 6 • DECEMBER 2009

WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

Hachinski Elected Next WFN President

BY MARK HALLETT, M.D.
Editor in Chief

BANGKOK — The 19th World Congress of Neurology in Bangkok was a wonderful success. There were more than 4,100 delegates from 115 countries. The delegates profited from a rich scientific program and enjoyable social events. Many also took advantage of being in Bangkok, going on a variety of sightseeing tours of this interesting city. The first 2 days had teaching courses on various topics. Subsequently were 5 days of invited talks and new scientific platforms and poster presentations.

The Council of Delegates of the WFN had a meeting at the beginning of the congress. Dr. Johan A. Aarli presided in his last meeting as President. The first item of business was the election of the new officers. Dr. Vladimir Hachinski and Dr. Jagjit Chopra explained to the delegates why they should be elected the next president, and Dr. Werner Hacke, Dr. Leontino Battistin, and Dr. William Carroll explained why they should be elected the next vice-president. There was no presentation for Secretary-Treasurer General because Dr. Raad Shakir was the only candidate. The three candidates for a new trustee position did not make presentations. The delegates voted, and Past Presidents Jun Kimura and Lord John Walton of Detchant went to count the votes, while the business carried on.

COURTESY THAI ORGANIZING COMMITTEE

The World Congress of Neurology was opened by HRH Princess Maha Chakri Sirindhorn (seated, center), seen here with WFN officers, VIPs, and the Thai organizing committee.

After the lunch break, Lord Walton announced the winners: Dr. Hachinski, Dr. Werner Hacke, Dr. Raad Shakir, and Dr. Wolfgang Grisold as the new trustee.

Another item of decision was the site for the 2013 Congress, which by rotation is planned for Europe. The societies in the European Federation of Neurological Societies had gotten together and decided to put Vienna into nomination. No other nominations were submitted and Vienna won by default (but with considerable enthusiasm). For 2015, the meeting will be in the Americas, and bidding is now open.

As to membership in the WFN, there was happiness expressed that there is now representation from three Chinese societies, China, Taiwan, and Hong Kong, and representatives from all three were present—Dr. Chuan-Zhen Lu, Dr. Ching-Piao Tsai, and Dr. Raymond Cheung, respectively. In addition, three new countries—Albania, Al-

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INSIDE

New Techniques Highlight Longer-Term Effects of TBI

BY MICHELE G. SULLIVAN
Elsevier Global Medical News

BANGKOK — New imaging techniques may help to explain the disabling symptoms that can plague patients with traumatic brain injury long after their acute problems have resolved, and eventually guide the best choice for medical therapy.

Survivors of traumatic brain injury who complain of depression, irritability, and memory or cognitive problems are often written off as psychiatric cases or malingerers, Dr. Ramon Diaz-Arrastia said at the World Congress of Neurology. "This is the frustrating thing about TBI. The patients might look OK—they don't have paralysis; they are walking around. But their cognitive and behavioral problems are real."

Imaging techniques that are now well established in other areas of neurology—such as diffusion-weighted and susceptibility-weighted magnetic resonance imaging—are now being used to show that brain injuries leave permanent, life-altering marks behind after the contusions and hematomas have healed.

These findings may have both immediate and long-range benefits, said Dr. Diaz-Arrastia, a professor of neurology at the University of Texas Southwestern Medical Center, Dallas, Tex., U.S.A. "Right now, imaging these patients has the primary value of providing a prognosis and perhaps helping them obtain the care that they need. In terms of reimbursement, it's useful to have an objective documentation of the injury when trying to convince insurers to cover rehabilitative service."

In the future, imaging the post-TBI brain may help guide medical treatment choices and monitor drugs' effectiveness.

So far, nearly 30 drugs have

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EDITOR IN CHIEF'S COLUMN

Neurology for All the People

BY MARK HALLETT, M.D.

Bangkok — The World Congress of Neurology was impressive for several reasons. One was the obvious, that neurologists were there from all over the world. Participants came from over 115 countries and, because of extensive education programs, including from the Congress itself, the level of clinical neurological expertise is becoming similar everywhere. Plenary lectures, platform presentations, and abstracts came from all over the world. Neurologists in some parts of the developing world, because of heavy clinical loads, may well have more clinical experience with some types of patients than "experts" from the developed world. Neurologists in India, for example, will see more patients with Wilson disease than would movement disorder specialists in the United States. Generally speaking, the same neurological conditions are seen everywhere, although the proportions differ.

The goal of the WFN, as with most neurological societies, is to get good neurological care to all the people. This is where there are problems. Depending on the country, the problems are different both in type and magnitude. In the United States, the government is currently grappling with reorganizing the system to get even basic health care to everyone. Political and economic interests make the negotiations complex, but there are certainly enough resources. At the other end of the scale, there are many poor developing countries with only few, or even no, neurologists, and very limited resources and medications. What can be done in this type of situation? The WFN is taking on these problems. More neurologists have to be trained, and their level of expertise maintained. Neurologists on the ground, who work mostly in cities, have to find ways to deliver care to patients in the rural areas. For example, in Mongolia, almost all neurologists are in the capital city, Ulan Bataar, whereas much of the population are nomadic herders scattered around the country. Similarly, in many sub-Saharan African countries, many people are living in villages far from the cities and their medical schools.

Courtesy Dr. Mark Hallett

Dr. Mark Hallett, left, and Keith Newton, Executive Director of the WFN, at the opening reception of the World Congress of Neurology in Bangkok.

Neurologists can go out into the field, as Dr. Amadou Gallo Diop of Senegal does with his neuro-caravans, as he described at the Council of Delegates meeting and in one of the Congress sessions. Telemedicine might be able to play a role. Dr. Gretchen Birbeck of the U.S.A. has taken the approach, piloted in Zambia, of getting non-neurologist health workers trained in some basic neurological skills to deal with the most important and common problems.

In many of these situations as well, the neurologists have to cope with treating patients without the availability of much equipment. MRI and even CT scanners may be sparse. A sole EEG machine cannot be helpful if it is broken or has no paper; a new digital model may be too expensive. To deal with epilepsy, there might only be phenobarbital available. Neurologists have to do the best they can and hope resources will improve. Each country has to ante up to help its own, but there are good opportunities for philanthropy to have immediate benefit. Dr. Diop could use his own van rather than having to rent one each time. With donations, the World Neurology Foundation can buy more neurological tool kits to help neurologists with their physical examinations. In World Neurology, we will try to keep you informed about what is going on in different countries. ■

TALK BACK

We're Waiting to Hear From You …

Do you want to share or report on something that interested you at this year's World Congress of Neurology in Bangkok?

Do you have an idea for a story?

Do you want to comment on something you've read recently in World Neurology?

Or perhaps you'd like us to share news of your research or upcoming event with the global neurology community.

Send us an e-mail at worldneurology@elsevier.com

World Neurology

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

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

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

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

Global Medical Research
Publisher Peter F. Bakker

Elsevier Global Medical News
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RESEARCH GROUP REPORTS

The Many Facets of Organization and Delivery

The beginnings of the World Federation of Neurology's Research Group for Organization and Delivery of Neurological Services go back to the 1987 New Delhi preparatory meeting of WFN committees for the 14th World Congress of Neurology in 1989. At that meeting, Jagjit S. Chopra and I put forward a proposal to organize a symposium on "Neurology in Developing Countries," based on our experiences as neurologists in our own countries, India, and what was then Yugoslavia. The proposal was accepted, and the symposium took place 2 years later, with speakers from developing and developed countries making substantial contributions.

BY BOSKO BARAC, M.D., PH.D.

Dr. Barac is professor of neurology in the medical faculties of the University of Zagreb and the University of Osijek in Croatia. He is a member of the WFN Research Committee and was a founding chairman of the Research Group for Organization and Delivery of Neurological Services.

A draft of the meeting proceedings and resulting recommendations, titled "Resolution and the Recommendations on Neurological Services in Developing Countries," was approved by the WFN and published in several neurological journals. The Federation also established a new research group relating to neurology and neurologists and the organization and delivery of neurological services.

The late Prof. Richard L. Masland, who was then WFN President, and Lord John Walton of Detchant, then Chairman of the Research Committee, insisted that the optimal organization and delivery of neurological services were also a problem in developed countries and that the common goal of improving these circumstances worldwide was to be the mission of the whole WFN. The founding members, eminent neurologists from all over the world, supported the program of activities of the new group.

The research group was very active, with many meetings being held at numerous international neurological gatherings: at the Pan-European Congress of Neurology in Vienna in 1991; the Pan African Association of Neurological Sciences Congress in Marrakesh in 1992; the 15th World Congress of Neurology (WCN) in Vancouver in 1993; the 1st Conference on Organization and Delivery of Neurological Services (ODNS) in New Delhi in 1994; and the 2nd Conference on ODNS in Athens in 1996, among others.

At the Athens conference, the attendees summarized the problems in the delivery of neurological services worldwide, and the document was approved at a meeting between the research group and representatives from the World Health Organization (WHO) at the 16th WCN in Buenos Aires the following year. The officers and members of the group disseminated the information about its aims at various regional, national, or international conferences. At the 18th WCN in Sydney in 2005, members of the group requested funding for their quest to assist neurologists in various parts of the world in delivering quality neurological services.

Some of the issues and problems that were repeatedly stressed included:

- ▶ Urgently needed neuroepidemiological investigations;
- ▶ Infections and infestations as etiologic factors of neurological diseases in developing countries;
- ▶ The need for using appropriate screening measures in field studies;
- ▶ Sensitivity and specificity of modern technologies in terms of relative availability and diagnostic efficacy;
- ▶ The importance of subspecialties in specific fields of neurology;
- ▶ The need for a system of horizontally and vertically connected hierarchical organization of neurological services based on active primary health service, respecting local and regional situations;
- ▶ The appropriate education of neurologists in terms of modern scientific advances, but simultaneously for practical work in their specific conditions using rational diagnostic and management means;
- ▶ The perils of "copying" education and management models from the most advanced medical communities to the underdeveloped nations, with founding centers of excellence organized for specific regional needs; and
- ▶ The need to recognize the cost-benefit aspects of neurological management as a growing interest in the world neurological community.

Specific concerns were raised about recent developments in some health care systems—such as the emergence of health organizations, "rational-through-competition purchasing" of health services, and the fact that investors were profiting from the health systems. The research group maintained that such approaches to health care could be devastating in less developed countries and emphasized that the WFN in collaboration with the WHO should strive to prevent such developments.

Another area in which international collaboration is needed is neuroethics. This is important because of the need to study and address sensitive issues in neurology that sometimes are connected to religion to regional cultural traditions.

The closer collaboration between the WFN and the WHO should increase public and professional awareness of the importance of neurological diseases for public health worldwide.

Finally, I want to express my deep gratitude to the officers and members of our group; the organizers and speakers involved in our conferences, meetings, and symposia; and our founding members who continue to contribute their ample professional experience and human empathy in advancing the group's basic principles. I would also like to express a special gratitude to the WFN leaders, who stressed the importance of such work, and to my colleagues and friends who organized some of the meetings: Jagjit S. Chopra, Franz Gerstenbrand, Maynard M. Cohen, Helmut Lechner, Francisco Rubio-Donnadieu, and many others.

I hope that the ODNS group will continue with its activities, which are important for neurology as well the human community, under the leadership of the Acting Chairman, Dr. Leontino Battistin, and in future years. The leaders of the other research groups are invited to collaborate with the ODNS group to achieve the common interests of the WFN in the respective fields of neurology. ■

Spreading the Word on Sleep and Good Health

The Sleep Research Group of the World Federation of Neurology adopted a declaration during the 2nd World Congress of Sleep Medicine in Bangkok in 2007 recognizing that sleepiness and sleeplessness are a global epidemic that threatens health and quality of life.

The group asserted that much could be done to prevent and treat disorders of sleep and alertness—of which apnea, restless legs syndrome, and psychophysiologic insomnia are the most common—especially if it were initiated through professional and public awareness campaigns.

Findings suggest that sleep problems threaten the health and quality of life for up to 45% of the world's population (Aging Health 2008;4:11-21).

In addition to causing distress to the individual, sleep problems also create a significant burden on society. In the United States, it is estimated that direct and indirect costs of insomnia amount to $107.5 billion annually (Sleep Res. 1997;26:412). Yet despite the seriousness of the problem, less than a third of people with moderate to severe sleep problems seek professional help (Am. J. Managed Care 2007;13: S112-6).

BY ANTONIO CULEBRAS, M.D.
Chair, Sleep Research Group, WFN

Dr. Culebras is professor of neurology at the Upstate Medical University in Syracuse, N.Y., U.S.A.

Sleep deprivation has also been associated with decline in mental health, and people with insomnia are more likely to suffer symptoms of depression and anxiety (Sleep 1999;22: S379-85). Other links have been made between sleep deprivation and conditions such as hypertension, obesity, diabetes, and weakened immune system. Sleep disorders can also negatively affect overall quality of life and family and social relationships.

This year, the WFN Sleep Research Group underscored its commitment to raising global awareness of the importance of sleep when it endorsed World Sleep Day, on March 20. This annual event is organized by the World Sleep Day Committee of the World Association of Sleep Medicine. It aims to lessen the burden of sleep problems through better prevention and management of sleep disorders.

The slogan for 2009 was "Drive Alert, Arrive Safe." In the United States, up to 20% of road fatalities annually are thought be related to fatigue and tiredness. To reduce the risk of sleepiness on the road, the World Sleep Day message emphasized the importance of understanding what is needed to ensure wakefulness when driving.

Improved diagnosis and treatment of sleep disorders could also help reduce fatal or serious road accidents by up to one-third, says the World Association of Sleep Medicine. Insomnia, one of the most common sleep complaints, has been linked to a significant rise in road accidents.

Next year, World Sleep Day will be on March 19 and its slogan will be "Sleep Well, Stay Healthy." The aim will be to educate both adults and children on how to improve sleep quality.

The 2010 World Sleep Day committee is Allan O'Bryan, Ph.D., executive director; Antonio Culebras and Liborio Parrino, cochairs; Richard P. Allen; Teresa Canet; Sudhansu Chokroverty; Wang (Jenny) Fang; Christian Guilleminault; Suresh Kumari; Mohamed Masmoudi; Julia Santin; Garima Shukla; Robert Thomas; Claudia Trenkwalder; and Catesby Ware. ■

PRESIDENT'S COLUMN

A Federation of Clinical Neurosciences?

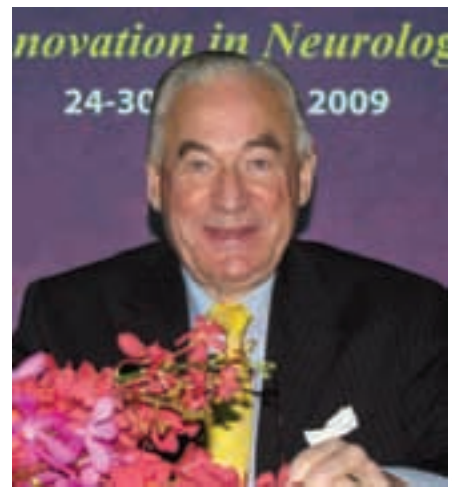
BY JOHAN A. AARLI, M.D.

The founders of the WFN in 1957 realized that collaborative international programs in clinical and basic neurological research would be central among the activities of the new organization. One of the first projects came through a grant from the National Institute of Neurological Diseases and Blindness (now the National Institute of Neurological Disorders and Stroke at the National Institutes of Health in Bethesda, Md., U.S.A.) to fund research on the geographical pathology of cerebral vascular disease.

The international research projects were dealt with by new organizational elements called "problem commissions," which were established in cerebrovascular disease, child neurology, tropical neurology, neurogenetics, neuromuscular disease, and many other areas of neurology.

Discussions were held about establishing a sister organization, a World Association of Neurological Commissions, with less formal links to the WFN. But the proposal met with major difficulties, and in 1966, the Federation established the Research Committee of the WFN.

The problem commissions became known as Research Groups, which were the building blocks of the Research Committee. Its first Chairman was Prof. Adolphe Franceschetti from Geneva. In 1977, Lord John Walton of Detchant was elected Chairman, and Prof. Armand Lowenthal was elected Secretary of the Research Committee. The WFN Council of Delegates decided the groups should raise funds to support their activities.



Courtesy Dr. Mark Hallett

Dr. Johan A. Aarli presided over his last meeting as President at the WCN 2009.

There are now 29 WFN Research Groups. Some, such as Cerebrospinal Fluid, Neuromuscular Disease, Neurogenetics, Neuro-Ophthalmology, Parkinsonism and Related Disorders, Tropical Neurology, and others date back to the days of the problem commissions; others have been established in step with developments in modern medicine.

Many WFN Research Groups have developed into new international societies and become corporate members of the Research Committee. Neurology has grown from a relatively well-defined specialty in the 1950s into one with a network of subspecialties and special interest groups with strong ties to other areas of medicine and science.

An important part of this evolution is the formation of new international societies and the emergence of regional and international congresses of subspecialties in the field. By focusing on selected topics of neurology, new platforms have been prepared for international research activities, crossing borders between specialties and expanding our knowledge of neurological disorders. The WFN is dependent on this apparently unbounded expansion; there should be no preservation of the status quo in neurosciences.

The World Congresses of Neurology, which from this year will be held biennially, aim to present a cross section of contemporary neurology, bringing all these activities as main themes and symposia so that participants will have the opportunity to be updated in general neurology.

At the same time, those who want a comprehensive presentation covering more than is possible in one out of five main themes at a World Congress and who are not able to attend both, might decide to seek an international congress that focuses on a single theme, such as epilepsy or stroke. This is important and is an element of the basis for the development in clinical neurosciences.

For all specialties and subspecialties, there is probably an upper limit for how many international congresses can be organized annually within one sector of medicine. Financial and technical aspects of planning conferences are substantial. Organizing congresses and attending them is expensive and time-consuming, and advances in video-conferencing are paving the way for attractive alternatives.

Subspecialties and branches of neurology also might serve as nongovernmental organizations at international organizations such as the World Health Organization. For national health politicians, however, neurology is first and foremost a part of medicine. In countries with only a few neurologists, there is no need for a fragmented neurology.

The purpose of the global initiative of neurology and public health is to increase professional and public awareness of the frequency, severity, and costs of neurological disorders and to emphasize the need to provide neurological care at all levels, including primary care. For scientific progress, a plurality is a *sine qua non*. For the public health issue, the clinical neurosciences should have one voice. ■

Neurologists Sit for First EU Board Examination

BY RENÉE MATTHEWS
Elsevier Global Medical News

Six candidates from several European countries sat for and passed the first European Board Examination in Neurology held in June at the European Neurological Society congress in Milan.

The examination was developed by the European Board of Neurology (EBN), a section of the Brussels-based Union Européenne des Médecins Spécialistes (UEMS), which represents national associations of medical specialists in the European Union (EU). The purpose of the examination is to standardize training for neurologists across the EU, said Dr. Wolfgang Grisold, president of the UEMS and EBN. Other specialty sections within the UEMS already have European board examinations.

"Europe has worked on a system of training by informal curriculum or time in a junior post with examination at entry—at least in the U.K.—but no certification boards or exit exam that assesses competence to practice as a neurologist. This examination is an attempt to standardize the competence of trainees before they are appointed to a senior post," said Dr. Alastair Compston, professor of neurology at the University of Cambridge (England).

The examination marked the culmination of 3 years of collaboration between the scientific committees of the European Neurological Society (ENS) and the European Federation of Neurological Societies (EFNS)—which drew up the examination and developed a question and case pool—and members of the department of medical education at Ege University in Izmir, Turkey, who performed the quality assessment. The groups were invited to participate by the UEMS-EBN. Funding for the projects came from the UEMS/EBN and the ENS and EFNS, and the Vienna Medical Academy oversaw the organizational aspects of the process.

The examiners and successful candidates gather after the first European Board Examination in Neurology during the ENS congress in Milan this past summer.

Eligible candidates must either be certified by their national society or at a stage in their residency where they would be admitted for their national training certification. The examination is restricted to participants from EU member states. Initially, 12 candidates applied to take the examination—7 were admitted to sit for it, and 6 candidates eventually took it.

The examination consists of two compulsory sections and a third optional section for extra credit. The first part is a 2-hour, 120-question multiple-choice test based on the questions developed by the scientific panels of the societies. The second part is a structured oral examination focusing on four cases. After that, candidates can elect to do a 5-minute presentation of an interesting case or scientific research for extra points.

The ENB said it was not discouraged by this small number of candidates. It hopes numbers will increase and that the examinination will become a sought-after qualification that might eventually replace some of the national examinations.

There was a low take-up for the first examination "partly because individual countries are organizing their own domestic exams," Dr. Compston said. "It remains to be seen which system gains most momentum, but it seems certain that people entering training now will have to achieve this or a related local certification in due course, and in that sense it may be an important development."

Dr. Michael J. Aminoff, professor and executive vice-chair of the department of neurology at the University of California, San Francisco, and a board member of the American Board of Psychiatry and Neurology, said he suspected the examination would become "increasingly important. It is something that the American Board will need to monitor, especially if issues such as recognition, reciprocity, and so on, come up."

Dr. Svein Mellgren of the department of neurology at the University Hospital of North Norway in Tromsø is the chairman of the examination committee. The examiners were Dr. Andreas Steck of the University Hospital Basel and the ENS; Prof. Savas Ozturk of Ege University, and UEMS/ EBN; Prof. Laszlo Vecsei of the University of Szeged, Hungary, and EFNS; and Dr. Gareth Llewelyn of Cardiff, Wales, and UEMS/EBN. ■

Role of Olfaction Explored in Diagnosing PD

BY JOHN DUDA, M.D.

Olfaction, considered by some to be the neglected sense in neurology, was the focus of a symposium at the 6th International Congress on Mental Dysfunctions and Other Non-motor Features in Parkinson's Disease and Related Disorders held in October last year in Dresden, Germany.

Although olfactory dysfunction is more common in Parkinson's disease (PD) than is resting tremor—one of the cardinal features of the disorder—that was possibly the first time at a congress that a full symposium was dedicated to it.

Recent advances in research include the recognition that olfactory dysfunction might precede the motor symptoms of PD, and that the olfactory bulb and tract might be one of the induction sites for Lewy pathology. In addition, olfactory dysfunction has been found to have sufficient clinical utility that a recent evidence-based practice parameter from the American Academy of Neurology stated that olfactory testing should be considered to differentiate PD from some other atypical Parkinsonian disorders, including progressive supranuclear palsy and corticobasal degeneration.

ONE OF THE PRESENTERS, RICHARD DOTY, PH.D., DISCUSSED HIS RECENT DATA ON THE PREVALENCE OF SMELL DYSFUNCTION IN WELDERS.

It was with this in mind that the members of the program committee of the Dresden meeting decided to include a session titled: "Olfaction and Parkinsonism: What we know and how you can use it in your clinic," to review recent advances related to olfaction and PD.

The session included several luminaries in the field, including Richard Doty, Ph.D., of the University of Pennsylvania, who had one of the first reports linking olfactory dysfunction and Parkinson's disease in 1988. He presented his recent data on the prevalence of smell dysfunction in welders with occupational exposure to manganese that suggested that 88% of these welders had poorer smell function than age-matched controls.

Another prominent contributor to the field from Barts and the London School of Medicine and Dentistry, Dr. Christopher Hawkes, discussed his observations of olfactory dysfunction in PD and normal aging, which suggest that PD starts with an acute event and progresses faster than simple aging.

Dr. Thomas Hummel, from the University of Dresden Medical School, Germany, summarized the modalities available to assess olfaction, including his own work with Sniffin' Sticks, which combines assessments of odor identification, odor discrimination, and odor detection threshold, and which he helped develop. I reported my recent findings on the use of the olfactory system as a pathological model of Lewy neurodegeneration.

Dr. Henk Berendse of the VU University Medical Center in Amsterdam rounded out the symposium with a discussion about the possibility of using olfactory dysfunction as a biomarker of early nonmotor PD. Data from a prospective study in asymptomatic first-degree relatives of PD patients at his institution have shown that otherwise unexplained olfactory deficits are associated with a 10% risk of developing PD within 2 years.

Spurred by the attendees' enthusiasm about the symposium, the presenters said they wanted to continue to raise awareness of the role of the neglected sense as a tool in the clinical evaluation of movement disorder patients and in PD research. A follow-up session on this topic is planned for the 7th International Congress on Mental Dysfunctions and other Non-Motor Features in Parkinson's Disease and Related Disorders to be held Dec. 9-12, 2010, in Barcelona, Spain. ■

DR. DUDA is director of Parkinson's Disease Research, Education and Clinical Center, Philadelphia VA Medical Center and assistant professor of neurology at the University of Pennsylvania School of Medicine, Philadelphia.

Patent Foramen Ovale in Vascular Neurology

BY ALEXANDER Y. GUR, M.D., PH.D.

Dr. Gur is a senior neurologist in the Stroke Unit in the neurology department at Tel Aviv Sourasky Medical Center and a lecturer at Tel Aviv University's Sackler Faculty of Medicine.

BY NATAN M. BORNSTEIN, M.D.

Dr. Bornstein is head of the Stroke Unit in the neurology department at Tel Aviv Sourasky Medical Center and a professor at Tel Aviv University's Sackler Faculty of Medicine.

The foramen ovale is a remnant of fetal circulation resulting from incomplete closure of the interatrial septum. Usually, fibrosis follows complete fusion of the interatrial septae by the age of 2 years. However, if there is no septal fusion, it will result in patent foramen ovale, a potential one-way valve for the right-to-left shunting that can permit the systemic passage of thrombi of venous origin into the intracranial circulation and which can result in paradoxical embolism.

Patent foramen ovale (PFO) was first described in 1564 by the Italian surgeon, Leonardi Botallo, and in 1877, Julius F. Cohnheim, a German pathologist, was the first to describe the occurrence of paradoxical embolism through a PFO in an autopsy study.

Seeing the Problem

Today, PFO can be visualized noninvasively by transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), or by transcranial Doppler (TCD) recording of microemboli tracks.

For detection of right-to-left shunting (RLS) through the PFO, the agitated saline is injected intravenously during these procedures at rest and after a Valsalva maneuver. TEE remains the "gold standard" tool for PFO documentation, with 91% sensitivity and 99% specificity, compared with TTE, which detects 50%-60% of PFO. The sensitivity of TCD for PFO monitoring is estimated at 84%-92%, and in some series has been superior to TEE in detecting small PFOs and quantifying cerebral RLS. Nevertheless, TEE allows for the direct measure of the PFO diameter and exploration for additional atrial and aortic sources of emboli. (The mean diameter of PFO is 4.9 mm [range, 1-19 mm], which is sufficient to allow passage of emboli large enough to occlude the middle cerebral artery trunk [3 mm] and major cortical branches [1 mm].)

Atrial septal aneurysm (ASA) is another interatrial septal abnormality that may interact with PFO. It is described as a hypermobile septum primum that protrudes alternatively into the right and left atria during each cardiac cycle. PFOs are detected in 20%-35% of the general population at autopsy or during TEE and might have a familial predilection with autosomal dominant inheritance. The prevalence of isolated ASA in the general population is less than 1% as measured by TEE but up to 83% of patients with ASA also have an RLS.

In addition to predisposing patients to paradoxical embolism, PFOs have also been implicated in cryptogenic stroke, migraine, platypnea-orthodeoxia syndrome, decompression illness in scuba divers, cerebral fat embolism syndrome, obstructive sleep apnea, and transient global amnesia. Paradoxical embolism is thought to be the mechanism of stroke in patients with PFO, because small blood clots could cross the PFO, leading to clinically significant sequelae in the brain. The "lurking clot" theory suggests that thrombi could form within the PFO tunnel (in situ PFO thrombus). Despite intensive work-up, more than 40% of all ischemic strokes have no clearly identifiable cause and are classified as cryptogenic.

Cryptogenic Stroke and Pelvic Veins

In 1988, two case-control studies reported an increased prevalence of PFO in patients with cryptogenic stroke (40%-50%), compared with controls (10%-15%). Prevalence was also higher in patients in the cryptogenic stroke group than in those with a determined origin of stroke (45% vs. 23%, respectively). Calculations based on these findings suggest that in the United States, about 100,000 strokes a year could be attributed to PFO.

A meta-analysis suggests a strong relation between PFO and cryptogenic stroke, especially in patients who are younger than 55 years. In addition, the combined presence of ASA and PFO significantly potentates stroke risk in these younger patients. Although most case-control studies of PFO and stroke have focused on patients under the age of 55 years, at least in one study, the risk of having a PFO in the setting of cryptogenic stroke has been confirmed to be higher in older patients as well.

Not all cases of cryptogenic stroke with PFO paradoxical embolism must be assumed as a stroke mechanism. To be able to suggest a true causative relationship between a PFO and cryptogenic ischemic stroke, several inquiries should be made about sedentary period or Valsalva maneuver before the stroke of onset. Straining at stool, heavy lifting, sneezing, coughing, vomiting, sexual intercourse, and other activities associated with Valsalva maneuvers and higher intrathoracic pressure make paradoxical embolism more plausible. Indeed, prolonged immobility as in car or air travel ("economy class" stroke syndrome) or immobilizing procedures are more likely to lead to thrombus formation in the deep or superficial veins.

Pelvic veins are an important source of paradoxical embolism in patients with PFO. In the Paradoxical Emboli from Large Veins in Ischemic Stroke (PELVIS) study, pelvic deep vein thrombosis (DVT) as detected by magnetic resonance venography was more frequently presented in patients with cryptogenic stroke and PFO than in those with stroke of determined origin (20% vs. 4%, respectively). Patients with postulated paradoxical embolism appear to have a large PFO (more than 2 mm in diameter); a large RLS magnitude; and coexisting ASA, DVT, and prothrombotic disorders. Furthermore, embolic stroke neuroimaging and clinical topography support the paradoxical embolization mechanism in patients with cryptogenic stroke in whom PFO is detected.

Management Strategies

To date, management of patients with PFO and cryptogenic stroke presents a clinical dilemma for neurologists and cardiologists. Strategic options for the prevention of recurrent stroke in these patients include antiplatelet or anticoagulant therapy, or surgical or percutaneous closure. On the one hand, the PFO in Cryptogenic Stroke Study (PICSS) data support equivalent protective effect of antiplatelet and anticoagulant therapy in patients with PFO and cryptogenic stroke. On the other hand, surgical treatment can permanently close the PFO, thus eliminating the need for medical therapy, however, surgical closure requires thoracotomy and cardiopulmonary bypass with possible morbidities that include atrial fibrillation, postpericardotomy syndrome, and others.

There has been great technological advancement of the minimally invasive endovascular techniques for PFO closure, two of which, CardioSEAL (NMT Medical Inc., Boston, Mass., U.S.A.) and Amplatzer (AGA Medical Corp., Golden Valley, Minn., U.S.A.), have been approved by the U.S. Food and Drug Administration.

At least five randomized clinical trials are underway to compare PFO closure devices with best medical management to prevent recurrent stroke. Meanwhile, as long as there are no evidence-based medicine guidelines, a stratification of patients with presumed PFO-related stroke to different therapeutic regimens can be done according to individualized "decision-making strategy." ■

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FROM THE WCN 2009

A Platform for Scientific Rigor and Professional Exchange

The outgoing President of the World Federation of Neurology, Dr. Johan A. Aarli (2nd from right), is shown with the newly elected officials, from left, Dr. Werner Hacke, Vice-President; Dr. Raad Shakir, Secretary-Treasurer General; and Dr. Vladimir Hachinski, President.

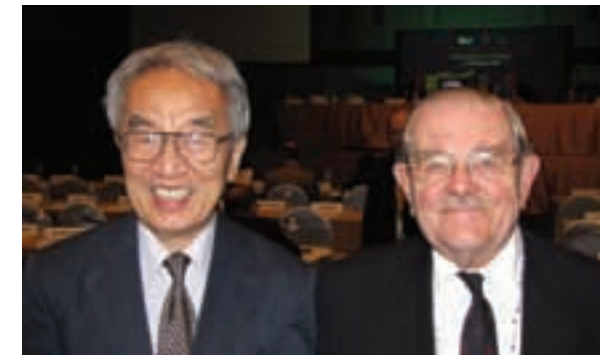
From left are Dr. Niphon Poungvarin, president of the Congress; Dr. Chuan-Zhen Lu from China; outgoing WFN President, Dr. Johan A. Aarli; Dr. Ching-Piao Tsai from Taiwan, and Dr. Raymond Cheung from Hong Kong.

Dr. Noshir Wadia of India was awarded a medal in recognition of his service and contributions to international neurology and the WFN.

Dr. Roger Rosenberg was awarded a medal for Scientific Achievement. His work has focused on the molecular biology of Alzheimer's disease.

Nobel laureate, Dr. Stanley Prusiner, presented his pioneering work on prions.

Dr. Niphon Poungvarin was President of the 2009 World Congress of Neurology.



Dr. Jun Kimura and Lord John Walton of Detchant, both Past Presidents of the WFN, were the vote counters in the elections for new officers, held at the Council of Delegates during the Congress.

PHOTOS COURTESY DR. MARK HALLETT

Next WCN in Morocco

WFN • *from page 1*

geria, and Kazakhstan—were admitted to membership at the meeting.

Dr. Aarli described activities with the World Health Organization (WHO). There is now a full-time neurologist there, playing a key role in the new subgroup of Psychiatry, Neurology, and Substance Abuse. There are special efforts to deal with the problems of epilepsy and dementia. There is also a push to get neurologists to teach the neurological curriculum at all medical schools; this does not happen now in countries where neurologists are few. The WHO is also responsible for preparing the ICD 11. Dr. Shakir is the chair of the neurology committee for the ICD 11, and Dr. Donna Bergen is the WFN representative to that committee.

Dr. Aarli also reported on the Africa initiative. Neurology courses have been given in Dakar, Senegal, and Addis Ababa, Ethiopia, and more are planned. Dr. Amadou Gallo Diop from Senegal described his "neuro-caravans," which he and other neurologists from the city use periodically to go into rural areas, where there are no neurologists, to help train medical workers there and to do some neurological consultation. This might be a model for other African countries.

Dr. Shakir reported that the finances of the WFN are in good shape and noted that the details of the balance sheet are posted on the WFN Web site.

The Opening Ceremony took place on Sunday evening, Oct. 25. The Congress was honored by the presence of HRH Princess Maha Chakri Sirindhorn, who formally opened the Congress. Dr. Niphon Poungvarin, the President of the Congress, and Dr. Aarli, gave introductory remarks, thanking the Princess. Then the Princess, noting the importance of neurology, declared the Congress open. Following was some entertainment, a performance of special Thai puppets, and then a welcome cocktail and buffet.

The Monday morning plenary session began with a presentation by Dr. Stanley Prusiner, a Nobel Prize winner, who presented his pioneering research on prions. He pointed out that it is possible to think about Alzheimer's disease and Parkinson's disease as being caused by pathological processes analogous to those of the classic prion diseases, such as Creutzfeldt-Jakob Disease. His new work includes studies of possible therapies. The second presentation was by Dr. Hachinski dealing with vascular disease of the brain. He pointed out how common vascular disease is and that neurologists should be alert to dealing with the modifiable risk factors.

After these two presentations, Dr. Shakir presented the first two WFN medals. Dr. Noshir Wadia of India received a medal for service to international neurology and the WFN. He developed one of the first academic departments of neurology in India and trained many neurologists active today. He was a founding member of the WFN Commission dealing with Tropical Neurology, and is well known for his work for the disabled. He has served on many WFN committees over many years, including Long Range Planning and Membership, and was the recent chair of the Nominating Committee.

Dr. Roger Rosenberg was awarded a medal for Scientific Achievement. Dr. Rosenberg, who is the director of the Alzheimer's Disease Center at University of Texas Southwestern Medical Center in Dallas. Dr. Rosenberg's early work led to the understanding of the genetic basis of Machado-Joseph Disease, now referred to as SCA3. For many years, he has been investigating the molecular biology of Alzheimer's disease and recently has developed a vaccine with significant therapeutic potential. His book, The Molecular and Genetic Basis of Neurologic and Psychiatric Disease (Philadelphia: Butterworth-Heinemann, 2003), is now in its fourth edition. He serves as editor in chief of the Archives of Neurology.

The delegates from Morocco are hard at work already planning the 20th congress in Marrakesh in November 2011. ■

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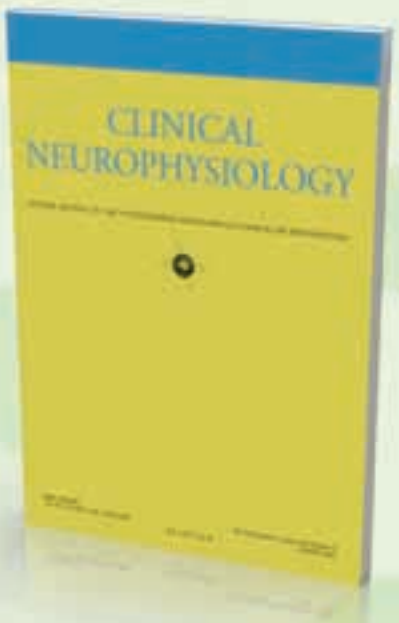

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MRS of Peritumoral Tissue Sheds Light on Biology

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

Compression of brain tissue by an external mass has many clinical effects, such as weakness, numbness, and seizures. How precisely these are caused by the tumor is not completely understood.

There are a number of possibilities, apart from direct compression of the brain by the tumor. The most obvious is edema, but other possibilities include ischemia because of compression of ambient microvasculature, elaboration of biologically active substances from the tumor, and direct microscopic invasion at the tumor-parenchymal interface. These are impossible to study in vivo, and so we need to turn to advanced imaging methods to help characterize them. Understanding these effects is useful because

Lip was also increased in symptomatic larger tumors that had more edema and were located in the skull base.

DR. CHERNOV

clinical management can be tailored to the individual tumor and it tells us about the basic biology of the effects of compressive brain tumors.

Dr. Mikhail Chernov and his colleagues in Tokyo took 100 patients with meningiomas and characterized the surrounding tissue by proton magnetic resonance spectroscopy (MRS), which measures the relative concentrations of various molecules in the tissue in a noninvasive way (J. Neurol. Sci. 2009;284:168-74).

These molecules reflect very sensitively the metabolic activity and structural integrity of the tissue, and localized lesions typically are compared with distant normal brain tissue. Thus, very roughly, the concentration of *N*-acetylaspartate (NAA) reflects the structural and metabolic integrity of neurons, choline (Cho) reflects membrane turnover, myoinositol reflects astrocytosis, mobile lipids (Lip) reflect necrosis and myelin disruption, and lactate reflects anaerobic metabolism. These are well-characterized metabolites that have been studied in other brain diseases.

In proton MRS, a small volume of interest ("voxel") is chosen, and the spectrum derived from MRS is analyzed for the metabolites of interest. The authors chose voxels of 3.4 or 8.0 mL, located not farther than 1 cm from the tumor margin. The results of MRS were correlated with size, degree of edema, and histopathology.

They found clear-cut changes in the peritumoral parenchyma by MRS in a limited number of metabolites. The NAA content in the peritumoral tissue was decreased by roughly 10% in the presence of peritumoral edema, compared with the distant normal-appearing brain parenchyma. This was more prominent in larger symptomatic tumors.

Of interest was that Lip was also increased in symptomatic tumors that were larger, had more edema, and were located in the skull base. Other metabolites were less prominently changed. Cho was relatively preserved in skull-based meningiomas but significantly decreased in other locations.

Other correlations were noted with symptoms, size, and edema, and with the histology and invasiveness of the tumor. Thus, invasive tumor growth was associated with lower NAA and Cho concentrations. The authors also derived an integrated score of metabolite abnormalities, which can be used to summarize sensitively the degree of abnormality.

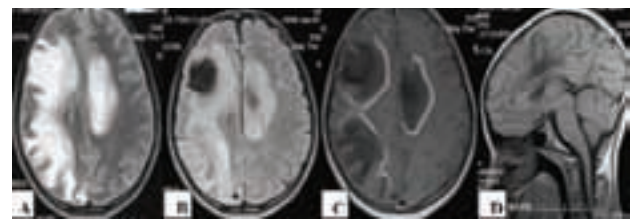
Dr. Chernov trained in St. Petersburg in Russia, where he completed medical school in 1989 and his neurosurgical training in 1995, after which he had visiting fellowships at Queen Square in London and the M.D. Anderson Cancer Center in Houston, Tex., U.S.A. He did a neurosurgical fellowship at the Tokyo Women's Medical University from 2002 to 2007, with a doctoral thesis on proton MRS of metastatic brain tumors and how these changed after gamma knife radiosurgery. He is assistant professor at the Tokyo Women's Medical University. ■

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

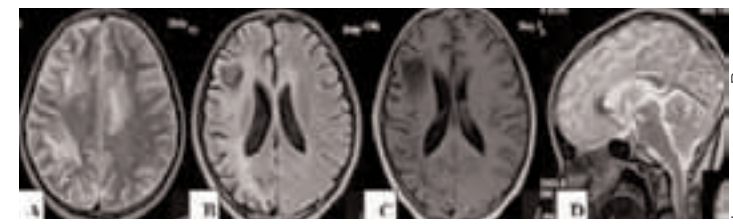
CASE STUDY

Watch for Tuberculous Encephalopathy in Endemic Areas

BY SISAY GIZAW GEBRE-MICHAEL, M.D.; MELKAMU DESSIE ADEB, M.D.; AND YOHANNES WOUBISHET WOLDEAMANUEL, M.D.



Brain MRI showed a white matter lesion and cystic degeneration with free fluid and ring-like enhancement.



Anti-TB therapy reduced the lesions' size (A, B) and gadolinium enhancement (C) but the corpus callosum lesion persisted (D).

IMAGES COURTESY PIONEER DIAGNOSTIC CENTER, ADDIS ABABA, ETHIOPIA

Introduction

Mycobacterium tuberculosis as a cause of diffuse inflammatory white matter cerebral lesion was initially described in 1958 in India (Dastur et al., Acta Neuropath. 1966;6:311-26). This relatively rare condition, labeled as tuberculous encephalopathy, is characterized by predominantly demyelinating lesion with extensive inflammatory element in diffuse or multifocal areas of the central nervous system (Dastur et al.). In the current study, we describe a case of tuberculous encephalopathy and discuss the relevance of a therapeutic trial in diagnosing this rare disorder in a resource-limited setting.

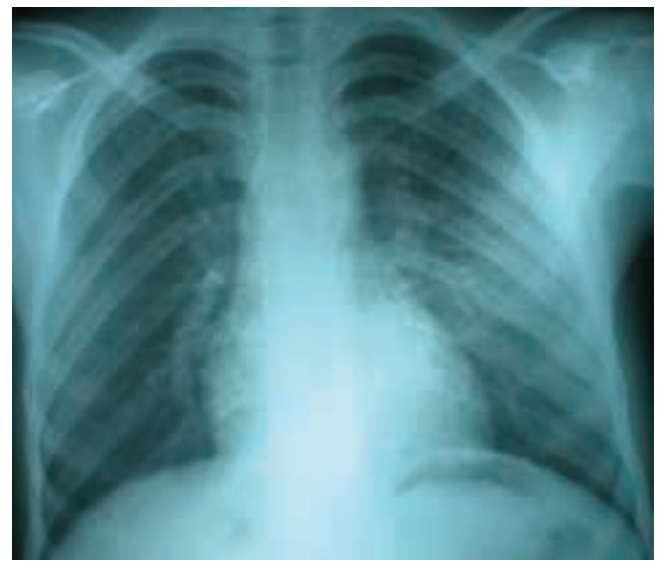
Case Report

A 13-year-old girl presented to the department of neurology at the Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia, with a 3-week history of bilateral progressive weakness with sequential involvement of the right upper limb, the right lower limb, and the left upper limb. She also developed weakness of left lower facial muscles and urinary incontinence. There were no symptoms of involvement of cognitive, language, visual, or sensory functions, disturbance of consciousness, nor symptoms referable to other organ systems.

A month before onset of her current illness, she had an acute episode of global headache, projectile vomiting, neck pain and stiffness, low-grade intermittent fever, and brief spontaneous inappropriate laughing, all of which improved with a 1-week course of oral doxycycline 100 mg twice daily for a presumptive diagnosis of endemic typhus. She was fully immunized, had adequate nutritional history, and normal vital signs. She had had no contact with a known open pulmonary tuberculosis patient or person with similar illness. Family history was negative for neurological or neuromuscular disease.

There was a left supranuclear facial nerve palsy and slight leftward tongue deviation with a normal active motor function. Examinations of the other cranial nerves, including direct ophthalmoscopic evaluation, were normal. Her limb muscles had normal bulk and showed no abnormal involuntary movement. The right upper, the right lower, and the left upper limbs had significant muscle weakness and spastic muscle tone. She had a loss of vibration and position senses on the right side. Biceps, triceps, brachioradialis, quadriceps, and ankle muscle stretch reflexes were hyperreflexic on the right side with bilateral extensor plantar responses. She had right hemiparetic gait and posture.

Blood chemistry and urinary tests were normal. Hematologic studies showed leucopenia (3,200/μL, 54% neutrophils; 34% lymphocytes) and elevated erythrocyte sedimentation rate (62 mm/hr). Serum syphilis and HIV-1 testing were negative. A chest radiograph was normal. Magnetic resonance imaging (MRI) of the brain with and without gadolinium revealed multifocal exclusively white matter lesion with associated focal cystic degeneration containing central free fluid and peripheral ring-like enhancement in the hemispheres.



A chest radiograph showed normal left-side rib crowding and fine nodular densities in lower lobe of the left lung.

On the basis of local epidemiological grounds, and clinical and radiological evidence, we started her on a treatment trial for central nervous system (CNS) tuberculosis, tuberculous encephalopathy (TBE), with rifampicine, isoniazide, pyrazinamide, and ethambutol (category I regimen 2RHZE/4RH, daily) along with a 60-mg oral prednisone tablet. After 2 weeks of treatment she started to show clinical improvement despite discontinuing prednisone on day 10. The muscle weakness and urinary incontinence improved. In the seventh week of treatment, she completely recovered from her neurological deficit and showed marked radiological improvement on brain MR.

Discussion

TBE is characterized by predominant signs and symptoms of diffuse cerebral involvement in the absence of large multiple cerebral tuberculomas with or without accompanying features of tuberculous meningitis (TBM; Dastur et al.).

One review found TBE to be a widely recognized disease entity with immune and nonimmune underlying etiopathogenetic mechanisms (Lammie et al., Acta Neuropathol. 2007;113:227-34). They suggested TBE shows a close clinicopathologic resemblance with a spectrum of immune brain disorders such as acute disseminated encephalomyelitis and experimental allergic encephalomyelitis, and an epidemiologic and perhaps etiopathogenetic relationship with diffuse (Schilder type) or acute (Marburg type) variants of multiple sclerosis. Dastur et al. said the neuropathological findings of TBE also are heterogeneous, but consistent features include diffuse and/or patchy, mostly white matter edema, demyelination, axonal loss, and variable astrogliosis.

TBE predominantly occurs in children and has variable clinical course ranging from fulminating or acute, rapidly fatal cases to subacute or chronic presentation with or without evidence of active extraneural tuberculosis or recent history of initiation of antituberculous drug therapy at the time of diagnosis (Dastur et al., Lammie et al.). It can manifest with several clinical syndromes, including TBM with encephalopathy, serous meningitis with encephalopathy, encephalopathy without meningitis, and acute hemorrhagic encephalopathy (Lammie et al.).

Diagnosis of CNS tuberculosis should be based on one culture-positive specimen (cerebrospinal fluid [CSF] or neural tissue) or by the presence of histological or clinical evidence of active CNS tuberculosis, along with a decision by a clinician to treat with a full course of tuberculosis chemotherapy (British Infection Society [BIS] Guidelines, December 2008). CSF and neural tissue specimen acid fast bacillus stain and nucleic acid amplification test remain the best rapid diagnostic methods for CNS tuberculosis, according to the guidelines. The difficulty and risk of obtaining stereotactic brain biopsy and lack of sufficient sensitivity of available diagnostic tests means that bacteriological confirmation usually is not possible and the diagnosis of CNS tuberculosis is often presumptive, the guidelines say.

Bacteriological study of autopsy and necropsy specimens of TBE consistently failed to reveal presence of mycobacterium in cerebral lesion (Dastur et al.). Besides delayed antituberculosis treatment of CNS, tuberculosis is strongly associated with death and neurological sequelae, and an empirical therapy is required in patients with possible CNS tuberculosis even before mycobacterial culture result is known (BIS Guidelines; American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America guidelines for treatment of tuberculosis, 2007).

In resource-limited countries, diagnosing CNS tuberculosis is even more difficult and needs an alternative approach. In the presence of strong clinical evidence of active CNS tuberculosis and background high tuberculosis prevalence, tuberculosis risk factors and additional suggestive laboratory features, including tuberculin skin test, CSF adenosine deaminase, interferon-gamma release assays, and brain MRI, might justify an empiric full course of tuberculosis chemotherapy (BIS Guidelines). Skin testing is variable (patients from high tuberculosis prevalence areas are more likely to have positive tests with unrelated illness). MR spectroscopy has shown the most promise in differentiating CNS tuberculoma from other causes of ring-enhancing brain lesions (BIS Guidelines).

Although therapeutic response is a bad diagnostic aid, diagnosis of CNS tuberculosis can be inferred from clinical and radiological improvement consistent with response to treatment, and the regimen can be continued to complete the standard course of tuberculosis chemotherapy (ATS/CDC/IDSA).

The incident case presented with clinical and radiologic features suggestive of TBE with complete clinical and significant radiological improvement with antituberculosis treatment. The prevalence of tuberculosis and rarity of alternative diagnoses also supported our clinical diagnosis of TBE.

Conclusion

In resource-limited countries with high prevalence of tuberculosis, the diagnosis of CNS tuberculosis, including TBE, can be made with compatible clinical and radiologic features and improvements to antituberculosis chemotherapy. ■

DR. GEBRE-MICHAEL *and* DR. WOLDEAMANUEL *are with the department of neurology at Addis Ababa (Ethiopia) University.* DR. ADEB *is with the university's department of radiology.*

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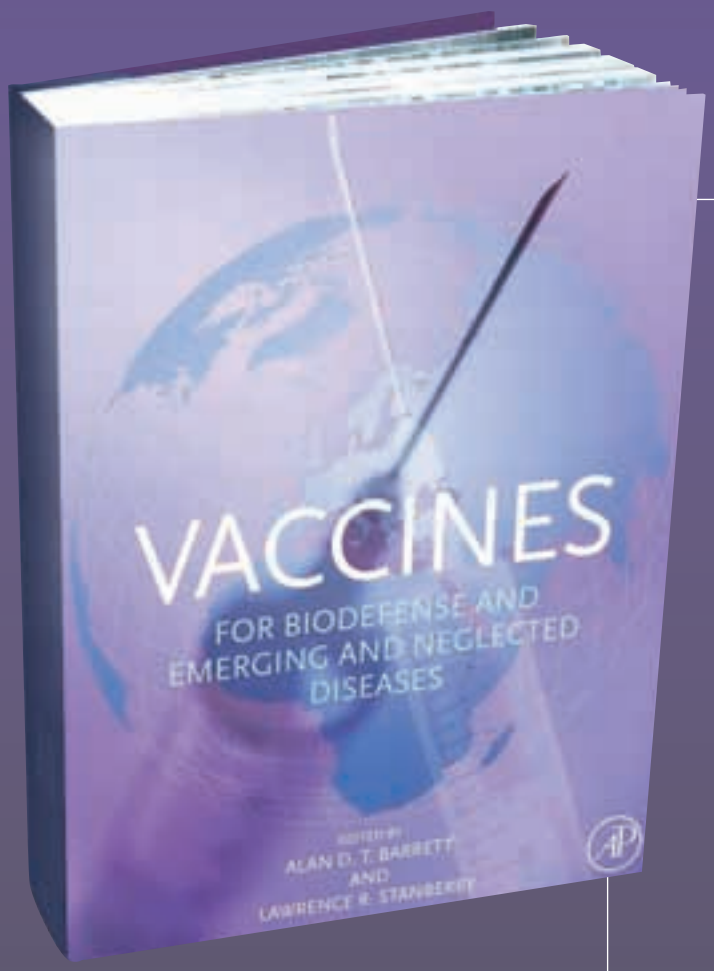

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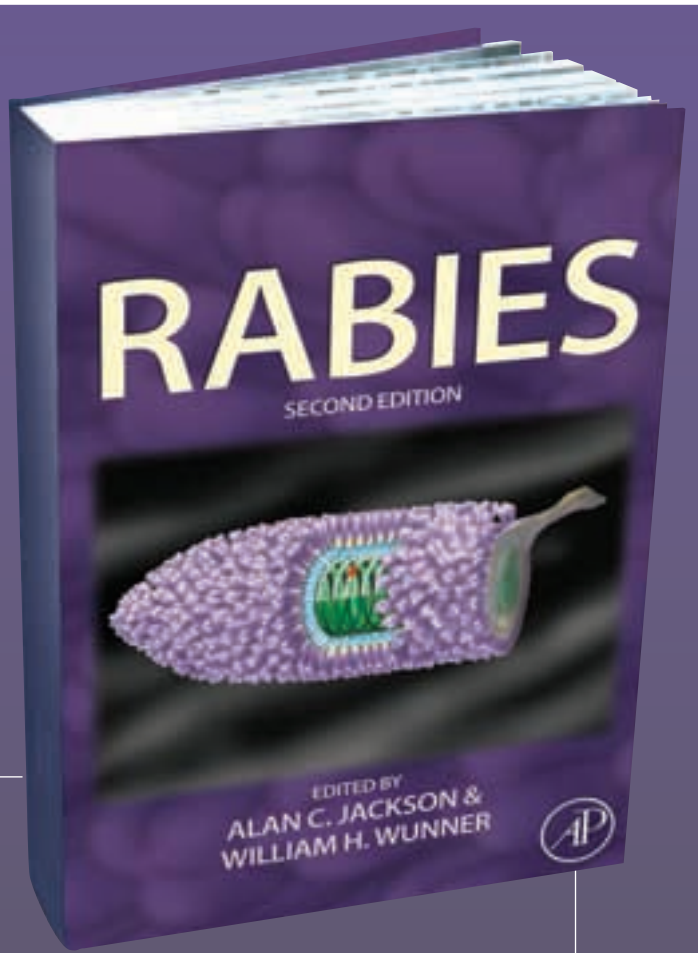

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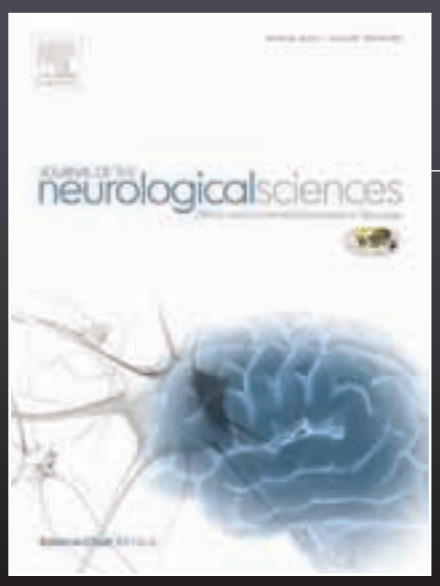

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Inhaled Migraine Drug Quickly Relieves Pain

BY MICHELE G. SULLIVAN
Elsevier Global Medical News

PHILADELPHIA — An inhaled form of dihydroergotamine provided significant relief of migraine pain, with sustained pain reduction and few adverse events, according to a phase III, placebo-controlled trial.

The drug conferred 4 hours of pain relief on 65% of those who took it; by 48 hours later, 39% still reported pain relief, Dr. Stephen D. Silberstein reported at the International Headache Congress.

Dihydroergotamine has traditionally been used in both an oral form and as an infusion for migraine. The inhaled version passes directly into the bloodstream through the lungs, working much more quickly, said Dr. Silberstein, director of the Jefferson Headache Center at Thomas Jefferson University in Philadelphia. It also bypasses the possible problem of nauseous patients vomiting an undigested tablet.

The FREEDOM 301 study randomized 903 patients with severe, recurrent migraine to either a placebo inhaler or to the inhaled dihydroergotamine; 792 were included in the intent-to-treat analysis. Their mean age was 40 years; their Headache Impact Test-6 score was 66, indicating severe disability. Most (91%) were women. At baseline, 54% characterized their migraine pain as severe, and 46% as moderate.

The study consisted of a 28-day washout period, during which patients kept a daily headache diary, followed by 8 weeks of randomized treatment. Two additional 8-week, open-label, follow-up trials are underway.

The primary end point was pain relief at 2 hours. A pain curve separation began at 30 minutes after dosing, but the groups were not significantly different at that time. At 1 hour, differences became significant, with 48% of the active group and 28% of the placebo group reporting relief.

'Triptan-like adverse events were rare, with rates in the active group comparable with those in the placebo group.'

DR. SILBERSTEIN

At 2 hours, pain relief was present in 59% of the active group and 35% of the placebo group—a significant difference. Significantly more patients treated with dihydro- ergotamine than with placebo had sustained pain relief at 24 hours (44% vs. 20%) and 48 hours (36% vs. 17%).

Freedom from pain was an important secondary end point. Again, significantly more of those taking the study drug were free of pain at 2 hours (28% vs. 10%), 4 hours (39% vs. 17%), 24 hours (23% vs. 7%), and 48 hours (18% vs. 6%).

Treatment with dihydroergotamine also significantly increased the percentage of patients who were free from phonophobia, compared with placebo (53% vs. 34%). Significantly more patients who received the drug reported being free from photophobia as well (47% vs. 27%). The drug had no significant impact on nausea—67% of the study drug group and 59% of the placebo group were free of it.

Adverse events were mild and occurred in 25% of the placebo group and 31% of the study drug group. Upper respiratory infections, sinusitis, and nasopharyngitis occurred in similar numbers. The most commonly reported adverse event was a complaint about the medication's taste. "Triptan-like adverse events were rare, with rates in the active group comparable with those in the placebo group, "Dr. Silberstein said.

Dr. Silberstein also presented several subanalyses examining the drug's effect in harder-to-treat groups. It reduced pain in 60% of those without baseline allodynia and 58% of those with baseline allodynia, and it relieved pain in 40% of those with morning migraine—a group that is sometimes medication refractory. It was significantly more effective than placebo when taken any time in the migraine cycle, but most effective when taken within the first 1-4 hours.

The study was sponsored by MAP Pharmaceuticals Inc., which hopes to market the inhaled formulation of dihydroergotamine under the trade name Levadex in the United States. Dr. Silberstein disclosed that he has received grants and honoraria from the company and has also been an advisory board member or consultant. ■

Comment

DR. STOVNER

These results are intriguing. However, it would be preferable to determine in a comparative study how well inhaled dihydroergotamine performs in relation to the triptans. If the results are borne out in practice, then the rapid onset of action, propitious side effect profile, and relatively low tendency for recurrence will be highly appreciated by patients. As with the triptans, one must expect that some patients will overuse the medication. I hope detoxification from dihydroergotamine will be less problematic than it is with the ergotamines. I also find it interesting that a relatively old drug like dihydroergotamine may get a second life with a new mode of administration. From a health economics point of view, it appears rational to use the full potential of existing drugs. Hopefully, this trend will not occur at the sacrifice of the development of even more innovative drugs and treatments.

—LARS J. STOVNER, PH.D., *professor of neurology and head of the department of neuroscience and the Norwegian National Headache Centre at the Norwegian University of Science and Technology, Trondheim.*

Imaging Could Help Prognosis

TBI • *from page 1*

provided effective neuroprotection in animal models of TBI, he said. However, none that has undergone testing in well-designed phase III trials has proven beneficial to humans.

Part of the problem may be the heterogeneity of human brain injury, Dr. Diaz-Arrastia said. There are many subtypes of TBI, yet "from the point of view of the clinical trials, all patients who present in a coma [after a brain injury] are treated the same way, even though the injuries can be very different, with very different prognoses."

Susceptibility-weighted imaging (SWI) is one technique being studied in TBI patients. It measures the paramagnetic shift of intravascular deoxyhemoglobin and methemoglobin, amplifying the appearance of microhemorrhages and making them much easier to identify. "SWI picks up 640% more lesions and 200% more lesion volume than does gradient-recall echo," Dr. Diaz-Arrastia said, referring to work by Dr. Karen Tong from Loma Linda (Calif.) University, U.S.A.

SWI is very good at identifying diffuse microvascular injury, a marker for diffuse axonal injury that is usually invisible on computed axial tomography. "The only problem is that SWI may be overly sensitive," he said. "One patient with a lot of microhemorrhages might be complaining only of headache and dizziness, whereas another with a similar volume might have a lot more problems."

Diffusion-weighted imaging (DWI), which is well established in the stroke world, is understudied in TBI, probably because it's a challenge to perform magnetic resonance imaging on these acutely ill patients. But this technique provides detailed information about the makeup of lesions, showing vasogenic and cytotoxic edema, as well as location in the superficial or deep structures in both gray and white matter.

Dr. Diaz-Arrastia and his colleagues performed DWI on 99 patients with TBI. Of these, the study identified corpus callosum lesions in 84%. It was able to differentiate between patients with primarily cytotoxic lesions (54%) and those with vasogenic lesions (46%).

"We also found that the volume of these brain lesions, irrespective of location, explained about 28% of the variance in outcome among these patients," he said. "It's a relatively modest correlation with outcome, but it shows that what we are measuring is something that is functionally important and affects outcome."

Diffusion tensor imaging (DTI) shows how water tracks along the axons, giving a good view of white matter lesions. Follow-up scans on TBI patients have shown tantalizing clues to the possible causes of their long-term problems.

Imaging provides objective documentation to help convince insurers to cover rehabilitative services.

DR. DIAZ-ARRASTIA

"When we scan patients within a day or two of injury, we may see subtle changes in the parameters. But if we come back 6 months later and rescan, we see much greater dropout of axons. Initially, the patient may be in a coma, and when they are scanned later they are usually much improved and walking around, albeit with problems with memory or executive function. So this tells us that something is happening weeks or months after the injury that results in white matter dropout."

Another technique moving into trauma field is quantitative volumetric assessment of the cortical field. This technique measures the thickness and volume of different cortical and subcortical regions, Dr. Diaz-Arrastia said. "In our patients, we have found that the brain shrinks overall after a severe traumatic injury, but that not all structures shrink at the same rate. Some cortical regions shrink very little, while others, like the hippocampus, appear particularly sensitive to injury."

This finding makes sense given the cognitive and mood issues that TBI patients can experience, he added.

On average, whole brain volume and both gray and white matter volumes decreased by 3%-10% in the first few months after severe TBI. In comparison, Dr. Diaz-Arrastia said, the rate of atrophy for patients with Alzheimer's disease is about 1%-2% a year.

Functional MRIs also provide some clues that the injured brain sustains long-term problems. In the resting state, the blood oxygen level dependent signal typically shows seemingly random fluctuations when the brain is at rest. But recent studies have shown that these fluctuations actually represent the communication between brain regions that work together.

"In our patients, we found a very high indication that the functional connectivity between the hippocampi was greatly reduced," compared with controls, he said. ■

Calendar of International Events

2010

Luxor International Symposium on Epilepsy and Movement Disorders
Jan. 13-15
Luxor, Egypt
www.neuroluxor2010.com

Neurology Update Mumbai 2010
Feb. 19-21
Mumbai, India
www.neurologyupdatemumbai.com

3rd International Congress on Gait and Mental Function
Feb. 26-28
Washington, D.C.
www2.kenes.com/gait/pages/home.aspx

3rd International Conference on Hypertension, Lipids, Diabetes and Stroke Prevention
March 4-6
Berlin
www.kenes.com/strokeprevention

Eighth World Congress on Brain Injury
March 10-14
Washington, D.C.
www.internationalbrain.org/?q=node/16

6th World Congress for Neurorehabilitation
March 21-25
Vienna
www.wcnr2010.org/

Twentieth Meeting of the European Neurological Society
June 19-23
Berlin
www.congrex.ch/ens2010

14th Congress of the European Federation of Neurological Societies
Sept. 25-28
Geneva
www2.kenes.com/efns2010/Pages/home.aspx

7th World Stroke Congress
Oct. 13-16
Seoul
www2.kenes.com/Stroke/Pages/Home.aspx

2nd European Headache and Migraine Trust International Congress
Oct. 28-31
Nice, France
www2.kenes.com/ehmtic/Pages/Home.aspx

14th World Pain Clinic Congress & 1st Asian Congress on Pain
Oct. 28-31, 2010
Beijing
www2.kenes.com/wspc/Pages/Home.aspx

MEETING ROUNDUPS

Parkinson's Experts, Patients Mix It Up

BY MADHURI BEHARI, M.D.

The 2nd Asian and Oceanian Parkinson's Disease and Movement Disorders Congress (AOPMC) and the 7th International Symposium of the Asian and Pacific Parkinson's Association (APPA) were held in New Delhi, India, in February.

The gathering was hosted by the New Delhi–based All India Institute of Medical Sciences and The Movement Disorder Society (MDS) at the city's India Habitat Centre. It was supported by the World Health Organization, the Indian Academy of Neurology, the Delhi Neurological Association, and the Delhi Ministry of Health and Family Welfare.

The AOPMC was attended by 330 delegates from India and abroad. The APPA was attended by 97 patients and an equal number of caregivers, and 189 allied health workers, such as nurses, physiotherapists, occupational and speech therapists, social scientists, and nutrition and diet specialists. An additional 37 physicians registered for the educational course, and 54 faculty members, comprising the invited speakers and the chairpersons, came from the Asian-Oceanian region, India, the United States, and the United Kingdom.

It was the first time a congress specifically for neuroscientists, researchers, persons with Parkinson's (PWP), their caregivers, and allied health workers was held in India, and the mix of attendees provided a unique opportunity for them to interact. The content material spanned the range of movement disorders, including chorea, tremors, progressive supranuclear palsy (PSP), multisystem atrophy (MSA), corticobasal ganglionic degeneration, psychogenic movement disorders, and dystonias.

The mix of attendees, from experts to PWP, presented a unique opportunity for them to interact.

DR. BEHARI

At the 2nd AOPMC, there were two industry-sponsored sessions on major areas of movement disorders—continuous dopamine stimulation and botulinum toxin for the management of dystonias and other hyperkinetic disorders.

Two breakfast sessions focused on an update on tremor and chorea and an overview of PSP and MSA. There were seven plenary sessions, including four on movement disorders in Asia, dealing with Lubag syndrome, a dystonia-like genetic disease specific to the Philippines; dystonia in Asia; infections and movement disorders; and metals and movement disorders, with particular emphasis on iron-related disorders and Wilson's disease, which is prevalent in India.

Another plenary session, on interventions in Parkinson's disease, covered recent developments such as deep brain stimulation and cell-based and gene therapy in Parkinson's disease. An educational course on managing Parkinson's disease covered its diagnosis, early versus late treatment with levodopa, autonomic disturbance and its management, motor complications and their management, psychosis and depression, and optimizing long-term therapy.

The 7th APPA program had two parallel sessions—2 half-days for PWP and their caregivers, and 2 full days for allied health personnel. Dr. Mary Baker, past president of the European Parkinson's Disease Association spoke about treating PWP in Europe and the role of caregivers. There were four sessions for PWP and five sessions and three highly interactive workshops for allied health personnel.

It was a matter of great honor that Dr. Kiran Walia , the minister of health and social welfare of the National Capital Territory of Delhi inaugurated the APPA conference. The AOPMC was inaugurated by Dr. Anthony E. Lang, president of the MDS. ■

DR. BEHARI is professor and head of the department of neurology at the All India Institute of Medical Sciences in New Delhi, India. She served as president and chairman of the organizing committee for this joint meeting.

Asian, Oceanian Neurophysiologists Gather

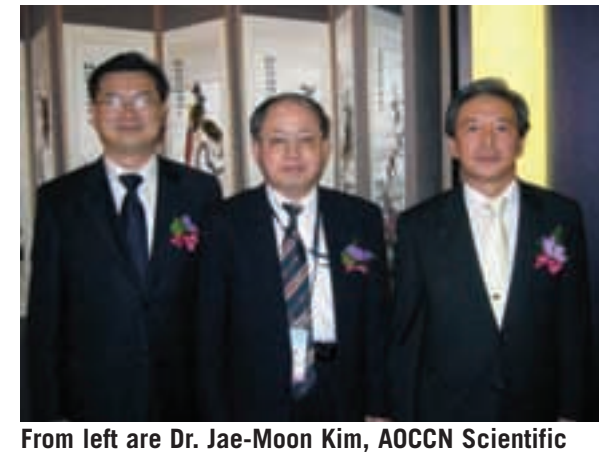
BY KWANG-WOO LEE, M.D.

As chairman of the organizing committee of the 2009 Asian and Oceanian Congress of Clinical Neurophysiology, I would like to thank everyone for joining us at the congress in Seoul earlier this year.

The theme of the gathering, which was hosted by the Korean Society for Clinical Neurophysiology, was "AOCCN in Cultural Variety: Momentum of Revival." About 700 specialists in clinical neurophysiology from 37 countries participated in the congress.

There is a growing global interest in neuroscience. With the rapid advancement in technology and bioengineering, the field of clinical neurophysiology is constantly changing and expanding, and it is important that specialists in related fields are able to gather to share the latest research data to ensure that everyone keeps current. This year's AOCCN provided us with these opportunities by acting as a hub of exchange for the field of clinical neurophysiology.

The program for the 3-day congress included plenary lectures, workshops, meet-the-expert panels, symposia, and 236 presentations on internationally relevant topics in neurophysiology. Participation was eager, and the quality of the presentations—some of which were landmark—and the ensuing discussions reflected the dynamism of the field.



COURTESY DR. MARK HALLETT

From left are Dr. Jae-Moon Kim, AOCCN Scientific Committee chair; Dr. Juhan Kim, Korean Society of Clinical Neurophysiology president; and Dr. Kwang-Woo Lee, AOCCN Organizing Committee chair.

Of the many superb abstracts presented, I would highlight two as they introduced new concepts or clinical applications: one, from Dr. Hae-Won Shin of Yonsei University College of Medicine in Seoul and colleagues, dealt with interhemispheric transfer of paired associative stimulation-induced plasticity in the motor cortex; another, by Dr. Joy Vijayan of National University Hospital in Singapore and colleagues, explored using combined Doppler and B-mode sonography to diagnose carpal tunnel syndrome.

It was an honor to host such a highly regarded international conference. I hope that in the future the AOCCN will be able to incorporate Europe and the Americas into its primary area of activity. I wish to express my deepest gratitude to the members of the organizing committee, and to the members of the AOCCN, the executive members of the International Federation of Clinical Neurophysiology, and our sponsors. I look forward to meeting you all again in 4 years' time at the next AOCCN in Bali, Indonesia. ■

DR. LEE was chairman of the organizing committee for the 2009 Asian and Oceanian Congress of Clinical Neurophysiology held in Seoul in April. He is professor of neurology at Seoul National University.