

WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

WFN ELECTIONS 2009

Candidates' Statements for President



JAGJIT S. CHOPRA,
FRCPE, PH.D., FAMS, FIAN

Introduction

I have served the World Federation of Neurology in various capacities for almost 25 years and plan to continue serving it with the same dedication and devotion. I am grateful to the WFN Nominating Committee for considering my candidacy for the office of President.

Having worked as a neurology teacher, researcher, and clinical neurophysician for almost 5

decades and having spent most of my life in a developing nation, I know what it is like to live in a society where people have no access to neurological services. As a result, I understand the extent to which neurological education and services are needed in developing and underdeveloped countries.

My main aim as President will be to strengthen both of these essentials—education and services—in developing countries and to raise awareness of neurology. I am eager to bring all member countries of the United Nations into the WFN fold and to maintain its close ties with the World Health Organization, American Academy of Neurology, and European Federation of Neurological Associations.

Background

I was born in India in 1935 and graduated in medicine from Punjab University in 1959. I

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VLADIMIR HACHINSKI, C.M., M.D.
FRCPC, D.SC., DR. HON. CAUSA

Introduction

The sharply rising prevalence of neurological disorders worldwide and the dismal global economic situation pose unprecedented challenges for the World Federation of Neurology. However, difficult times foster innovation and cooperation. I believe that the WFN will continue to thrive if we encourage greater participation, seek partnerships, and focus on

opportunities.

Background

I was born in Ukraine and raised in Venezuela. I graduated in medicine and neurology from the University of Toronto, Canada. I studied cerebral circulation physiology at the National Hospital for Nervous Diseases at Queen Square in London, England, and followed that with a research fellowship at Bispebjerg Hospital in Copenhagen, Denmark. I returned to Toronto, where I began my career and was later appointed the Richard and Beryl Ivey Professor and Chair of the Department of Neurological Sciences at the University of Western Ontario in London, Canada.

I began the Controversies in Neurology section in the Archives of Neurology, which engages a range of contentious issues in current neurology and which has become the journal's most popular feature.

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INSIDE

From North America

The spread of animal rights protests in the U.S. and elsewhere highlight the need to raise public awareness of the value of such work and to ensure such acts are prosecuted.

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From Thailand

Dr. Johan A. Aarli, WFN President, and Dr. Raad Shakir, the Secretary-Treasurer General, visited Bangkok, venue of this year's world congress.

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From Malawi

In 2008, Malawi opened its first MRI service and acquired the country's only scanner for its 13 million people. Now it aims to boost its number of qualified radiologists.

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Suicidality Alert for AEDs May Do More Harm Than Good

BY MICHELE G.
SULLIVAN

Elsevier Global Medical News

For years, scientifically sound data have informed clinicians that patients with epilepsy have an increased risk of depression. But the U.S. Food and Drug Administration's recent warning of an increased risk of suicidal ideation in patients on anti-

epileptic drugs, and the European Medicines Agency's recommendation to disclose such risk in product information for some of the drugs, are based on much less rigorous data, and could do more harm than good, say several experts on epilepsy.

The FDA's decision, announced last December, requires manufacturers of any medication in the class of anti-

epileptics to add warnings about suicidal thoughts or behavior in prescribing information or labeling and to develop medication guides for patients.

"Following the initial FDA alert reporting increased suicidal ideation with anticonvulsant drugs, a number of my patients called to ask if they should discontinue their medications. They did not realize, as I did,

that although any risk of suicidal ideation was very small, the risk of stopping medications, with possible uncontrolled seizures, was much greater. Fortunately I easily convinced them of this, but I do have colleagues who report that some patients stopped medications," said Dr. Carl W. Bazil, professor of clinical neurology at Columbia University, New York.

The EMEA only recommended that the risks should be mentioned with the product information for the antiepileptic drugs (AEDs) levetiracetam, pregabalin, lacosamide, and zonisamide. The European agency also said prescribers should be advised to monitor their patients for suicidal ideation or behavior

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EDITOR IN CHIEF'S COLUMN



BY MARK HALLETT, M.D.

Risky Research and Sharing Stories

Carleton Gajdusek has died, and one of his students and colleagues, Lev Goldfarb, has written an obituary in this issue of *WORLD NEUROLOGY* (see p. 14). Carleton was brilliant and a very colorful character whom I got to know in the National Institute of Neurological Disorders and Stroke (NINDS) intramural program at the National Institutes of Health in Bethesda, Md., U.S.A. His lectures were incredible and spellbinding. Back in the days before PowerPoint, I recall one of his lectures when he had three screens—dual slides and a movie—all running simultaneously. He loved to tell stories, and he always lectured overtime.

It is worthwhile to consider the work he did in discovering a new class of infectious agents, which earned him the 1976 Nobel Prize for Medicine. In travels to the island of New Guinea north of Australia, he lived with the Fore tribe and studied tribe members who were inflicted with kuru disease. He characterized them clinically and pathologically, and then realized that cannibalism was a part of their funeral rituals. It was practiced in secret, but like a detective, he documented clear evidence of it in photographs. Then he conducted the important lab experiments that demonstrated that the disease was infectious and that

the properties of the infectious agent were unusual. His work opened an entirely new area of biology and medicine.

If he had embarked on his research today, would he have been able to get a grant do so? Was his work hypothesis directed? Could he have gotten funding for longer than 5 years? It is easy to imagine this being branded as "too risky." However, the NINDS intramural program took the risk for a potentially high payoff. Dr. Murray Goldstein, the director of NINDS, tells the story of how Carleton once needed transport to get around in the Pacific region in order to continue his work. He simply hired a ship and sent the bill to Dr. Murray—who paid it.

It makes one wonder if today's funding agencies have become too conservative and short sighted. Sometimes it seems that the requirement for preliminary data means that the work is already half done at application time. Many funding agencies have recognized this and are trying to find ways to bypass the conservative approach and identify some risky projects that might succeed. This is certainly difficult but well worth doing.

But back to Carleton, who was also the source of many stories. He was always crying wolf about how the mice in Bethesda were going to shed the virus that would unleash a plague of hemorrhagic fever with renal syndrome. The Hantavirus was unknown in the United States—except for that one mouse that his children caught on his property.

He also warned against eating lamb chops. So I was not surprised when he

called me in the late 1980s (I was wearing an administrative hat at that stage) to say that he had just been to England as a consultant and that it appeared that some cows had come down with a scrapie-like disease. He predicted that this was going to be big news, have important health consequences, and cost millions of dollars. I thanked him politely and then forgot about it, until the mad cow disease stories hit the press. He was right that time. (Actually, he was sort of right about the hemorrhagic fever with renal syndrome as well. Many years later, there was just such an epidemic in the southwestern United States.)

In thinking about Carleton, it occurred to me that one thing neurologists enjoy when they get together is swapping stories, often about old times, their mentors, or great teachers. Many of these exchanges are part of our oral tradition, but I thought it would be fun—and possibly even valuable—if some of those stories were put down on paper and sent to us for publication. So, as with my call for you to submit articles relating to our specialty, I also invite you to share a favorite story with us.

I am grateful to David Dawson who is kicking off this feature in the current issue. On page 4, he tells the story of Soma Weiss, the brilliant young doctor who diagnosed his own ruptured cerebral aneurysm in the days before the clinical pathological correlation was well known. This issue, we have our first Letter to the Editor—also on page 4. Keep those coming as well. ■

Calendar of International Events

6th Baltic Congress of Neurology

May 13–16
Vilnius, Lithuania
www.balcone2009.com

1st International Course on Pain Medicine

May 28–31
Granada, Spain
www.icpm.net

13th International Congress of Parkinson's Disease and Movement Disorders

June 7–11
Paris
www.movementdisorders.org/congress/congress09/

44th Annual Congress of the Canadian Neurological Sciences Federation

June 9–12
Halifax, Nova Scotia, Canada
www.cnsfederation.org

15th Annual Meeting of the Organization for Human Brain Mapping

June 18–23
San Francisco, Calif., U.S.A.
www.humanbrainmapping.org

Do you have an idea for a story? Do you want to comment on something you've read recently in *WORLD NEUROLOGY*? Or maybe 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@gmail.com. We'd love to hear from you.



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THE PRESIDENT'S COLUMN

The Case for Biennial World Congresses

The 19th World Congress of Neurology in Bangkok, Thailand, in October this year, will be the last of its kind. The congresses have been quadrennial since the World Federation of Neurology was founded in Brussels, Belgium, in 1957. The first congress was held in Rome in 1961, where member countries were invited to present bids for hosting the 1965 congress. The delegates chose Vienna, Austria, and ever since, the congresses have been held every 4 years.

Initially, quadrennial congresses were sufficient to keep pace with developments in clinical neurology, but the landscape changed with time. There was a rapid development of new therapies and advances in diagnostic and imaging techniques. New subspecialties and related fields of medicine emerged, and there was a greater need for world congresses to be more specialized and focused on areas such as Parkinson's disease, epilepsy, stroke, dementia, motor neuron disorder, multiple sclerosis, and headache.

During this time, there was also a general feeling that the WFN's visibility was diminishing and that holding biennial world congresses would raise its profile in the international community. This idea was discussed over successive WFN ad-

ministrations. One alternative was that the federation should retain the quadrennial congresses and hold regional conferences in the intermittent years. However, we realized it would be difficult to fully realize this plan. Nevertheless, the regionalization of neurology has become increasingly important.



BY JOHAN A. AARLI, M.D.

In 2006, the Vice-President, Prof. Vladimir Hachinski, presented a discussion paper on world congresses to the Trustees. He asked whether holding the congresses every 4 years was too infrequent to have any sustained impact on the community, particularly when neurological conditions and knowledge were increasing. He suggested the congresses move to a 2-year cycle.

There are potential advantages to switching to a shorter cycle—it could increase the impact of the federation at the regional level as well as boost its visibility globally. However, it could lead to a decrease in industry revenue and it might clash with regional congresses. Until now, national societies responsible for organizing the congresses have done so through a congress organizing bureau, which could vary from congress to congress. With biennial congresses, we will need a permanent congress organizer (PCO), and we'll also need to adjust the

WFN committee system to include a Congress Supervisory Committee.

The proposal of 2-year cycles was presented to the WFN national delegates at the Council of Delegates in Glasgow in 2006. Delegates presented their views and proposals and had until the next Council of Delegates, in Brussels the following year, to form their opinions. There, a clear majority favored biennial congresses, starting from 2011.

Soon after that, the WFN contracted a PCO, established the WFN Congress Supervisory Committee (WCSC), and compiled a schedule for future congresses.

We have decided to use Kenes International as our PCO for the first series of world congresses, starting with the preparation for WCN 2011. The WCSC is appointed by the Trustees on the recommendation of the WFN President. We also agreed on the following schedule for future world congresses: 2013 will be in Europe; 2015, in the Americas; and 2017, in the Asian-Oceanian region.

It was also decided in Brussels that the 20th WCN in 2011 should take place in Africa. At the WFN Council of Delegates in New Delhi in 2008, Marrakesh, Morocco, was selected as the venue. Preparations for that congress have already started, and a report will be presented at the Council of Delegates in Bangkok this year. We look forward to organizing future biennial world congresses. ■

On Reflection: Soma Weiss

Dr. Soma Weiss, a physician and biochemist, played an important role in academic medicine in Boston in the mid-20th century despite his untimely death at the age of 43.

Although he had not trained as a neurologist, he was acutely aware of the contributions of neurology to internal medicine, and of his many published papers, more than a dozen were about epilepsy, vascular disease of the brain, beri-beri, carotid sinus sensitivity, and other conditions with neurological import.

Dr. Weiss had studied physiology and chemistry in Europe before emigrating to New York when he was 21. Soon after arriving in the United States, he went to study at the Cornell Medical School in upstate New York, where he quickly established himself as a star pupil.

He continued his medical training at the Boston City Hospital as part of the Harvard Medical School academic program. After completing his training, he advanced rapidly in his field and succeeded Dr. Henry Christian as chief of the department of medicine at the Peter Bent Brigham Hospital and as Hersey Professor of the Theory and Practice of Physick, the oldest professorship at Harvard Medical School. His appointment to

this prestigious position, at the age of 39, was a striking testament to his brilliance.

Those who knew Dr. Weiss always commented on his enthusiasm, warmth, drive, and legendary teaching ability. His ward rounds were known to attract as many as 100 students and doctors. He



BY DAVID M. DAWSON, M.D.

Dr. Dawson has been on the staff of the Brigham and Women's Hospital since 1967 and is professor of neurology at Harvard Medical School, both in Boston, Mass., U.S.A.

would go from floor to floor, seeing as many patients as were presented to him.

In late December 1941, Dr. Weiss was returning by train to Boston from Washington. He was an adviser to President Franklin D. Roosevelt, and on this occasion planning for the civilian aspects of the war was the reason for his visit. During the trip, he experienced a sudden blinding headache, vomiting, and stiff neck. He himself diagnosed a ruptured aneurysm, which his physicians later confirmed.

Not every physician was familiar with the clinical syndrome of ruptured aneurysm in that era, which predated the

availability of imaging techniques and arteriography. But Dr. Weiss had studied the case of a woman who had died of an aneurysm at the Brigham the previous year. He may also have been aware that the first clinical description of the syndrome in the literature had been made from the Brigham in 1921, by the British neurologist Charles Symonds and American neurosurgeon Harvey Cushing.

Dr. Weiss was cared for at home and visited daily by one or the other of his junior faculty, John Romano and Charles A. Janeway. A friend, Dr. H. Houston Merritt, also attended. No neurosurgeon was consulted; in any case, surgical procedures for aneurysm were in their infancy at that time.

Dr. Weiss improved slowly, but after a restless night in January 1942 he had a second hemorrhage and died the next day. An autopsy showed an anterior communicating aneurysm, with rupture into the frontal lobes.

His death at such an early age, and at the beginning of his career at the Peter Bent Brigham Hospital, was widely mourned. Each year, in remembrance of his contributions as a teacher, clinician, and advocate for research, the Harvard Medical School hosts the Soma Weiss Student Research Day, at which students present their research. ■

LETTER

Dr. Albert Saiz and Dr. Francesc Graus discussed the pathogenic significance of autoantibodies against glutamic acid decarboxylase 65 in stiff person syndrome (WORLD NEUROLOGY, December 2008, p. 16).

Glutamic acid decarboxylase 65 (GAD65) catalyzes the synthesis of gamma-aminobutyric acid, and glutamic acid decarboxylase 65 autoantibodies (GAD65-Ab) could possibly alter the balance between excitatory and inhibitory neurotransmitters. However, GAD65 is located in the cytosol and is therefore not readily accessible to antibodies. Nevertheless, transfer of immunoglobulin G (IgG) from GAD65-Ab-positive stiff person syndrome (SPS) patients induces an SPS-like phenotype in rats (Ann. Neurol. 2007;61:544-51).

We have recently shown that GAD65-Ab from cerebrospinal fluid (CSF) are oligoclonal, mainly IgG1, has high avidity, and persists for years (Eur. J. Neurol. 2008;9:973-80). This suggests they are produced by clonally expanded B cells that have received T-cell help. Accordingly, we were able to clone GAD65-specific T cells from the CSF of three patients with, but not from a single patient without, prominent intrathecal synthesis of GAD65-Ab (J. Autoimmun. 2009;1:24-32). We therefore conclude that clonally expanded GAD65-specific B cells and T cells coexist intrathecally.

Dr. Saiz and Dr. Graus state that T cells have not been identified in some autopsy reports. This does not disqualify T cells from the pathogenesis of SPS. There are few histological reports, and some have indeed shown discrete lymphocyte infiltration (Clin. Neuropathol. 1986;5:40-6 and J. Clin. Neurosci. 2002;9:328-9). Moreover, absence of evidence is not evidence of absence: The clonally expanded B cells secreting GAD65-Ab to the CSF must reside somewhere. Lack of overt inflammation in CNS specimens may suggest that the inflammatory foci are small and few, rather than non-existent.

Intrathecal synthesis of oligoclonal IgG is a hallmark of MS. In MS, the mechanism of IgG production is difficult to study because the specificity of the oligoclonal IgG is largely unknown. The finding that clonally expanded B cells and T cells specific for the same autoantigen coexist intrathecally in SPS should encourage the study of T-B cell collaboration also in MS.

Trygve Holmøy, M.D.

Institute of Immunology, University of Oslo and the Department of Neurology, Ullevål University Hospital Oslo, Norway

Dr. Saiz and Dr. Graus reply: We agree with Dr. Holmøy's points. He provides interesting data on the need to study T-B cell collaboration. However, we cannot add any comment since our studies in this matter were clinical.

Welcome
to the



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on the website: www.wcn2009bangkok.com

Chopra

Elections • from page 1

trained as a neurologist in Belfast, Northern Ireland, and became a member and later a fellow of the Royal College of Physicians (Edinburgh, Scotland).

On my return to India, I established the department of neurology at the Postgraduate Institute of Medical Education and Research in Chandigarh, Northern India, where I trained many neurologists.

I have conducted extensive research, published more than 235 scientific manuscripts, and coedited two books, "Neurology in the Tropics" and "Textbook of Neurology." I was founder president of the Indian Academy of Neurology and a past president of the Neurological Society of India.

Honors

I have won numerous national awards for my work, including the Dr. B.C. Roy National Award.

My achievements have also been recognized by the American Academy of Neurology and the American Neurological Association, both of which have made me an honorary member, and by the Association of British Neurologists.

In 2008, the president of India awarded me the Padma Bhushan, one of the highest civilian awards.

WFN Activities

I was the Organizing Secretary for the 14th World Congress of Neurology in New Delhi in 1989. It was a great success, marking the first time we broke even with our costs—and turned a profit that helped fund the publication and mailing of *WORLD NEUROLOGY* from India.

I became a member of the WFN's Finance Committee and later, its Joint Chairman, and have also been a member of the Public Relations, the Publications and Website, the Structure and Function,

and the Stroke Affairs and Liaison committees. I cochaired the federation's research group on Organisation and Delivery of Neurological Services and was invited to participate in its Africa Project.

I was selected Editor in Chief of *WORLD NEUROLOGY* in 1999 and was instrumental in improving content quality and ensuring its timely delivery. I edited my last issue in March 2008. The newsletter has been the single force that unites neurologists globally, and I was proud to be associated with it.

Two key proposals I put forward at the World Congress in Sydney in 2005 have been implemented: The world congresses are now held every 2 years, rather than every 4; and the WFN has taken great strides to enroll new member countries, especially from Africa.

Goals and Objectives

I want to make a concerted and vigorous effort to have the WFN's global aims and objectives adopted by all of its member countries. I also want to maintain close ties with the World Health Organization and nongovernmental organizations to raise awareness of neurology and to strive for the promotion of neurosciences in countries with poor resources. This is the WFN's greatest challenge.

The financial position of the WFN has improved greatly, but I shall continue to focus on it and to tap manufacturers, pharmaceutical companies, and the wealthy for donations that can be used to help people—especially those in poorer communities who are suffering from neurological disorders. I shall also seek financing for the purchase of a permanent head office for the WFN.

Every neurologist is a leader and there should be equal opportunities for all members from all WFN regions. I'll ask the Council of Delegates to adopt this constitutionally, so that we can consolidate our commitment to working for a more dynamic, integrated future. ■

Hachinski

Elections • from page 1

Over the years, I have trained, hosted, or supervised more than 100 fellows, visiting professors, and observers from all continents. In addition, I have been a lecturer or visiting professor in more than 60 countries, particularly in support of colleagues in countries where there are few neurologists.

I am currently professor of neurology and distinguished university professor at the University of Western Ontario and editor in chief of the journal *Stroke*, the leading publication of its kind in the field.

I have begun publication of eight international editions of the journal as well as an author mentoring program to help authors from developing countries get their work published in international journals.

Honors

1988 Doctor of Science (Medicine), University of London, England, for "contributions in migraine, stroke, and dementia."

2000 Doctor of Medicine honoris causa, from the University of Salamanca, Spain, where I delivered an acceptance speech titled, "Neurognosis: A Proposal to Bring Together the Sciences and the Humanities Through an Understanding of the Brain."

2008 Named to the Order of Canada (Canada's highest civilian honor) for "contributions to the field of neurology, notably as a leading expert and researcher in the study of stroke and dementia."

WFN Activities

I was Canada's delegate to the WFN and Chairman of its steering committee for two terms, during which time the federation noted that I had "brought parity and fairness in the interrelationship of

the WFN with regional and national groups" (Citation, WFN diploma).

I have also served as WFN Vice-President for North America. In that capacity, I initiated the process that led to the world congresses being held every 2 years, each time in a different region of the world so as to have an impact on the host region's local economy and to be accessible to neurologists or future neurologists who might not be able to travel internationally. Holding the meetings every 2 instead of every 4 years, provides a platform for more vigorous activity and continuity between congresses.

I established a cooperative relationship with the International Brain Research Organization and helped persuade the group to match our Africa initiative funds. And finally, I was instrumental in the formation of a WFN resident and fellows' organization.

Goals and Objectives

► **To promote greater participation.** I plan to encourage participation in the activities of the WFN among the membership and delegates by finding out what their priorities, needs, and desired opportunities are, and to seek models of successful initiatives.

► **To prioritize.** I see a need to focus on projects with specific objectives, a definite timetable, and a feasible action plan.

► **To partner.** The WFN should continue to foster its relationship with the World Health Organization, and opportunities should be sought for partnerships and collaborations in education, training, and building infrastructures with other organizations worldwide.

The growing menace of neurological disorders demands our renewed, focused, synergistic efforts. The greatest risk is not failing, but failing to act. Let us act as if the future of the WFN depended on us, because it does. ■

Stopping AEDs Poses Greater Risk

Suicidality • from page 1

while being treated with those drugs.

"The suicidality warnings have made very little difference to our clinical practice," said Prof. Martin J. Brodie, director of the epilepsy unit at the Western Infirmary, Glasgow, Scotland.

"It is well known that around a third or perhaps even more patients with refractory epilepsy will have comorbid depression as part of a panoply of brain dysfunction. This is associated with a small increased risk of suicide. A number of antiepileptic drugs can produce depression in a small number of patients," Prof. Brodie said.

"As it stands, epileptologists have long been aware of the importance of checking for potential suicidality in this population. However, I do not routinely warn patients of the possibility when introducing a new antiepileptic drug."

On the surface, Dr. Bazil said that the FDA's alert does sound frightening: Patients receiving AEDs had twice the risk of suicidal behavior or ideation than that

of those taking placebo. But even with this doubling, the risk remained small—less than 0.5% of patients taking the drugs. Moreover, the FDA recommendation was based on a retrospective analysis of 199 separate AED trials. None of these trials was designed to examine the risk of suicidal ideation; instead, this information was collected during patient self-reports of adverse events.

These reports, determined by a series of open-ended questions posed by the investigator, have a notorious potential for bias. If the patient complains of one adverse event—depression, for example—the investigator will automatically ask more questions, including questions about suicidality. And because it's known that drugs always evoke more ad-

verse events than do placebos, once a patient reports an adverse event, investigators will have increased vigilance for others. Thus, an adverse effect—in this case suicidality—could be recorded more often in the drug group than in the placebo group, even if the rates were similar in the two groups, according to Dr. Bazil, who is a member of the speaker's bureau for UCB Pharma, Pfizer, and GlaxoSmithKline.

Although the risk of suicidality is small, the risk associated with stopping medications is much greater.

DR. BAZIL

very depressed after successful surgery. It's a reaction to an enormous life change that requires a lot of adjustment. Similarly, patients who improve on drug therapy may also become depressed, but this doesn't mean that the drug caused the depression, he said.

Finally, the FDA's meta-analysis lumped

together all the classes of AEDs, making no attempt to categorize drugs by different mechanisms. There is no way to determine if a specific drug, or class of drug, was significantly associated with an increased risk of suicidality. From a scientific standpoint, it's hard to believe that so many drugs with different methods of action could have the same effect. There is information from other studies suggesting that certain drugs do have the potential to increase depression, and therefore (possibly) suicidality, but the FDA alert covers this very diverse group as one class, with one risk, Dr. Bazil said.

"In the trials that generated the suicidality warning, both the active and placebo treated populations were taking one, two, or three baseline antiepileptic drugs. Accordingly, the cause and effect relationship is by no means clear," Prof. Brodie said.

In the absence of prospective study using specially validated psychological measures, physicians should make sure that patients understand this is not a high risk, and stress that these drugs are very safe when taken as directed, Dr. Bazil concluded. ■



WFN ELECTIONS 2009

Candidates' Statements for First Vice-President

Introduction

The prevailing discrepancies in the practice of neurology throughout the world present great challenges for the World Federation of Neurology. In Europe and North America, neurology has advanced substantially with the advent of modern technology and advances in research



BY LEONTINO BATTISTIN, M.D.

in molecular biology, and these advances translate into more accurate diagnoses and effective therapies for patients. But these considerable advantages are available to a relatively small percentage of the world's population—in many regions of Africa, Asia, and Oceania, the practice of neurology is either inadequate or simply not available.

Background

I was born in 1939. I received my medical degree from the University of Padua, and from 1967 to 1970, I was a visiting research fellow at Columbia University's Research Institute of Neurochemistry in New York, U.S.A. On my return to Italy, I was assistant professor in the department of neurology at Padua's medical school. After tenures as associate and then full professor in neurology, I was named director of the school's Neurological Clinic. In 2002, I became head of the department of neurosciences.

In addition, I have been a member of the financial committee of the European Federation of Neurological Societies; president of the Italian Society of Parkinson's Disease and the European Society for Clinical Neuropharmacology; and organizer and chair of world congresses on neurorehabilitation and clinical pharmacology.

WFN Activities

I have had the privilege of serving the WFN as a participant in the Parkinsonian & Related Disorders, the Dementia, and the Organization and Delivery of Neurological Services research groups; as a member of the federation's Nominating Committee; as its Vice-President for Europe; and as Organizer and Chair of its congress on Parkinson's disease in Rome in 1994.

Goals and Objectives

The federation faces many obligations as it contemplates the future. It needs to:

- ▶ Develop and expand the practice of neurology worldwide;
- ▶ Support educational programs;
- ▶ Cooperate with national and international health organizations, such as the World Health Organization;
- ▶ Establish a policy for providing training and a support network for young neurologists; and
- ▶ Promote neurological and neurorehabilitation centers.

I believe collaboration and collegial decision making and am ever mindful that we need to be realistic in executing projects in a timely manner and without wasting resources. To achieve these goals, I would work to:

- ▶ Strengthen the organization by engaging a professional agency;
- ▶ Adopt a policy of transparency and ensure that all information about its activities reaches its members quickly; and
- ▶ Hold congresses, teaching courses, and scientific events throughout the world. ■

Introduction

Over the last 10 years, I have seen the World Federation of Neurology expand its role to a truly global strategic organization and embark on sustained endeavors in education and advocacy. The most recent of these has been the Africa initiative. The WFN faces a considerable challenge to continue such initiatives,



WILLIAM M. CARROLL, M.B., B.S., M.D., FRACP, FRCPE

while at the same time not neglecting other regions such as Central and Southeast Asia and parts of Eastern Europe. In these financially straitened times, it is the internal strength of organizations that determine continued growth and influence. Successful use of modern communications can bolster our organization

by improving members' proximity to the organization and its leadership. The reformatted WORLD NEUROLOGY, modernized Web site, and move to a biennial world congress have begun this process.

Background

Below are listed some of the positions that I have held, or currently occupy, followed by a summary of my WFN activities, which I believe support my candidacy:

- 2008-present** Vice-President, Asian & Oceanian Association of Neurology
- 2007-present** Vice-President, Pan-Asian Committee for the Treatment and Research in Multiple Sclerosis
- 2004-present** WFN Director, World Neurological Foundation
- 2003-present** Editor (Asia & Pacific), Multiple Sclerosis
- 1998-present** Chair, Research Management Council of Multiple Sclerosis Research Australia
- 1996-2004** Neurology Editor, Journal of Internal Medicine
- 1992-2000** President and Councillor, Australian Association of Neurologists (now the Australian and New Zealand Association of Neurologists)
- 1988-present** Head, Department of Neurology, Sir Charles Gairdner Hospital, Perth, Australia.

WFN Activities

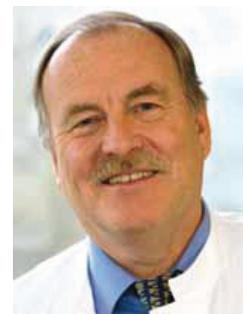
My association with the WFN began when I served as president of the Australian Association of Neurologists in 1999. At the 17th World Congress of Neurology in 2001 in London, I presented the successful bid for the AAN to host the 2005 18th World Congress of Neurology in Sydney. In 2001, I was also elected as a WFN Trustee and served two terms. As President of the 2005 World Congress of Neurology in Sydney, I was proud to be associated with its success, especially financially, with considerable funds accruing to the federation. I have chaired the WFN Fundraising Committee, and I serve on the Membership and the Publication & Website committees, as a member of the Editorial Board of WORLD NEUROLOGY, and as an invited member of the Task and Advisory Force for Neurology in Africa.

Aims and Objectives

- ▶ To enhance the WFN's ability to communicate with neurologists and neurological associations worldwide.
- ▶ To maintain existing initiatives in Africa and Central America and develop others elsewhere in the world.
- ▶ To develop an equitable formula for subscriptions for countries of differing economic circumstances.
- ▶ To cement the WFN's financial stability. ■

Introduction

My three main objectives as vice president of the World Federation of Neurology would be to improve neurological care and research; to ensure that the advances in the diagnosis and treatment of neurological diseases are made available in all regions of the



WERNER HACKE, M.D., PH.D.

world, and to make neurology visible in the field of medicine.

Background

I am a neurologist and a psychologist by training. I am 61 years old and have been chairman of the department of neurology at the University of Heidelberg (Germany), for more than 20 years.

My main interest areas of interest in neurology have always been stroke and critical care neurology, though I also have a major interest in higher brain functions and neuropsychology.

International Activities

During the past 20 years I have devoted much time to international teaching activities. Many delegates will know me from their national or regional neurology and stroke conferences, at which I have had the honor to speak.

I have received honorary membership from several neurological societies, including the American Neurological Association, the French Neurological Society, and the All-Russian Society of Neurologists.

Currently, I am president of the European Stroke Organisation and in the past, I have been president of the German Neurological Society, the German Stroke Society, and the German Society for Neurological Critical Care Medicine.

WFN Activities

I became involved in the WFN very early in my career. In 1995, I became secretary to the World Congress of Neurology (WCN) president, the late Professor Klaus Poeck. I was the founder and founding president of the WFN's Research Group for Critical Care Neurology.

In 2006, I became an elected trustee with the WFN, and I have worked actively on the Board of Trustees since then.

As the chair of the Conference Oversight Committee, I worked on the future structure of the WCN and its change to a biennial conference.

Goals and Objectives

- ▶ To continue to work on the new format of the World Stroke Conferences with special emphasis on geographic distribution and input.
- ▶ To pursue greater collaboration with our colleagues in neuromedicine—with neurosurgeons, neuroradiologists, neuropediatricians, and neuropathologists.
- ▶ To help raise the profile of neurology. Our specialty has not received the public attention it deserves as a discipline that works with our most precious organ. Considering the amount of funding and public interest that is given to cancer, AIDS, and heart disease, we have a long way to go.
- ▶ And most importantly, to promote teaching and training activities for neurologists in developing regions of the world and to support broader training and qualification program. ■

Neurologists in the Crosshairs

BY P. MICHAEL
CONN, PH.D. AND JAMES V.
PARKER, PH.D.

We don't know about you, but when we were choosing our careers, it didn't occur to us that we would find ourselves in the crosshairs of terrorism. We weren't becoming police officers, after all, or even high-earning bankers whose children might be at risk for kidnapping.

We were going to become researchers, which meant years of education and commitment to postdoctoral programs and residencies for the privilege of competing for meager federal funding from the U.S. government. We were picking a profession in which our goal would be to understand the workings of neural systems, so that we could help correct those defects—biochemical and anatomical—that cause disease.

In addition to benefiting humankind, we knew that animals would also benefit by the work that we were doing.

When we were students, extremist acts against animal research were happening only in England; they posed no threat to most researchers in the U.S.A. But that has changed. The British research community has succeeded in educating the public about the importance of its work and, because of that, the number of extremist acts has all but disappeared. In contrast, extremism against animal research has increased in other countries such as Europe, Canada and the United States, Asia, Australia, and South America.

Today, many of those engaged in neurological research are aggressively targeted by these extremists. Being targeted means having extremists coming to our homes with bullhorns and distributing pamphlets that claim that we torture animals. The leaflets include our home addresses and phone numbers with the gentle suggestion that the reader express "outrage" in what we do. Targeting means stalking our children and spray painting or firebombing our homes and cars.

These extremists demonize and misrepresent both what we do and its value. They distribute "educational" materials in many schools, claiming that our research is worthless and that researchers are actually engaged in federally supported animal torture.

How do we respond to this? We don't, thereby making ourselves the best of all possible targets: One that doesn't fight back. We work in our labs and clinics believing, wrongly, that the average person understands and appreciates the long hours and sacrifices we make to learn about neural systems, work that, as we have mentioned, is so essential to diagnosing, treating, and curing disease.

When we and our colleagues became targets of extremism against animal research, we were amazed that the public—and, in fact,

many of our colleagues outside of our state—were not aware of what was happening. We wrote a book, "The Animal Research War" (New York: Palgrave Macmillan, 2008), to raise public awareness of the benefits of research. We realized that young people, seeing what is happening to their mentors and observing the lack of public support, are making alternative career choices. Some of our colleagues quit productive careers out of concern for the well-being of their families.

The public buys medicines from drug companies, but because it doesn't understand the role of research in developing those drugs or in bringing them through safety testing and to market, it is prone to accept activists' arguments that the use of animals in drug development can be replaced by cell cultures or computers. The public seldom realizes that researchers actually developed these techniques and currently use them. But computers model only data, and cell cultures measure only part of the response of a living organism to a drug. Even if a drug were to come directly from cell culture, laws in the United States and in most countries require that drugs first be



Animal Liberation Front activists at a public protest (top) also left threatening messages at researchers' homes (bottom).

tested in animals before they can be used by humans. Most people don't understand the federal regulation of research; when they are told about that level of oversight, many become supportive of our efforts.

What can you do? Talk with nonscientists about what you do and show them your lab and animal facilities; they need to know about the benefits of the research and that your research is both humane and closely regulated. Offer to visit schools and have that same conversation with the students. Invite field trips to your institution and suggest age-appropriate projects that engage students in research.

We know that those activities may not help researchers get tenure or research funding. This means that if the "you" we are addressing is an administrator, consider giving incentives to your staff to encourage them to take part in an educational mission to guarantee the survival of animal-based health research. ■

DR. CONN is a scientist and administrator at the Oregon Health & Science University's Oregon National Primate Research Center in Portland, U.S.A. DR. PARKER is an ethicist and former public information officer at the research center.

COMMENTARY

BY JASPER R.
DAUBE, M.D.

The Task Force on Animals in Research of the American Academy of Neurology's Science Committee has been working for more than 20 years to raise awareness among neurologists and the general public of the growing threat of animal rights activists to neurological research.

Although the animal rights terrorist activity highlighted by Dr. Conn and Dr. Parker has shown a marked increase in the last 2 years, there is an even greater long-term threat to neurological research—activists' efforts to increase the legal rights of animals.

They hope eventually to grant animals "personhood." If that were to occur, then any interested party could bring legal action against researchers and institutions engaged in animal research. The increase in legal threats has come about in large part through the rapid expansion of courses in animal law at the major law schools in the United States.

The U.S.-based Society for

Neuroscience and other basic science-related organizations have been working through their animal research committees to raise members' awareness of these threats and help them and their institutions understand and respond to the threats.

However, some major medical organizations have not recognized the seriousness of these issues and have not warned their members or patients.

Much more needs to be done. This will not be an inexpensive task. Hundreds of millions of dollars are donated to animal rights organizations each year. A recent, single, television advertisement brought in U.S.\$30 million.

The World Federation of Neurology needs to recognize the gravity of this issue and develop programs to encourage medical organizations to join the efforts to bring the dangers of the animal rightists to the attention of their patients and the public. ■

DR. DAUBE is chair of the Task Force on Animals in Research of the American Academy of Neurology's Science Committee.

BY ROGER LEMON, PH.D.

It was with a strong sense of déjà vu that I read this very stirring article by Dr. Conn and Dr. Parker. Researchers and doctors in the United Kingdom have endured similar abuse from the so-called animal liberationists for many years.

My main comment would be that despite these setbacks and abuses, the scientific community must continue to work hard to improve openness about what we do and why we do it. We must continue to try to engage in a dialogue with those opposed to the use of animals in research.

However, this is only possible with those who agree to debate in a peaceful manner, and not with those who force their views upon others through violence and fear. The fear instilled in researchers by the illegal intimidatory actions is the main weapon of those anti-vivisectionists who cannot argue their case in a rational manner. Their actions are often better characterized by hatred of humans than love of animals.

This fear factor can only be overcome by making sure that these illegal acts are prosecuted. In the United Kingdom, the government has come to recognize the threat of these illegal and intimidatory acts, has brought in new legislation and strengthened existing laws, and ensured that

animal terrorists are prosecuted and put in prison.

This is undoubtedly why, in the United Kingdom, we have seen a steady reduction in the level of serious antivivisection violence. This has also come about because more and more scientists, doctors, and patients have articulated the need for animals to be used in research, and this has won over an increasingly large fraction of public opinion in favor of well-controlled animal research.

This debate, this battle is well over 100 years old and no doubt will continue. It is disturbing to consider that some of the tactics and violence developed in the United Kingdom have been exported to countries such as the United States and Germany.

However, researchers in those countries should be heartened by more recent developments in the United Kingdom. The battle against the extremists can be won by speaking up for our cause and emphasizing that what we do brings great benefit to both human and veterinary medicine, and that the many drugs and treatments that our society uses daily could not have been developed without animal research. ■

DR. LEMON is the Sobell Professor of Neurophysiology at the UCL Institute of Neurology at Queen Square, London.





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Countdown to the October Congress in Bangkok

BY JOHAN A. AARLI, M.D.
President, WFN
 AND RAAD A. SHAKIR, M.D.
Secretary-Treasurer General, WFN

In February, we made a routine visit to Bangkok, where this year's World Congress of Neurology will be held. The trip was part of the pre-congress arrangements and had been scheduled because we wanted to inspect the congress venue at Bangkok International Trade & Exhibition Centre and examine the transport facilities between the hotels and the center.

We also wanted to assess the impact of the global recession on international travel to scientific meetings. Our impression was that there is still a considerable amount of tourism to Thailand even though international air traffic volume is less than it was a year ago.

Bangkok's Suvarnabhumi airport was completed in 2006. The Suvarnabhumi Airport Project is a national priority and is intended to establish Bangkok as the aviation hub of the Southeast Asian region. Are there fewer passengers than usual? It is difficult to say. Our flights, from Copenhagen and from London on a Thursday, were full. We thought the airport was crowded, but there were no long queues.

Bangkok International Trade & Exhibition Centre (BITEC) was officially opened in 1997. It is a modern and unusually well-equipped conference center, with grand lecture rooms and excellent facilities for exhibitions, conventions, and special events—and more than adequate space for the poster presentations. In addition, there are 15 rooms for committee meetings.

We were also impressed by the large reception area, automatic teller machines and internet services, and facilities for handicapped persons. The 19th International

Congress of Nutrition, a much larger gathering than ours, will be held at the center from Oct. 4–9, just 2 weeks before ours, and the organization for both is running according to schedule.

There are few major hotels close to BITEC. Most are in the city center, and if one uses the mass transportation network, the BTS Skytrain, the trip from those hotels to the center will take 30–40 minutes, and a little more at rush hour. Most guests will probably first check in at their hotels and then find their way to the center. Some of the main hotels will operate shuttle-bus services to the center (schedule information will be posted on the congress Web site).

The Skytrain is fully operational, but unfortunately the final stretch to the center is not yet finished, so there will also be a shuttle-bus service between the Skytrain's last station and the center. Delegates to the congress will receive free tickets valid for 1 week.

All congress activities will take place at BITEC. Teaching courses and workshops will be held in the morning, before the scientific sessions, and will cover topics such as stroke, multiple sclerosis, epilepsy, dementia, movement disorders, and headache/pain. There will be several sessions for free communications and a daily debate session. And, as was the case in London 2001 and Sydney 2005, there will be a Tournament of the Minds, with the final taking place on Friday, Oct. 30. The opening and farewell sessions will be at the center, as well as the spectacular Thai Night on Wednesday, Oct. 28.

Another crucial issue that we addressed during our visit was related to Thailand's political situation. We met the secretary to Prime Minister Abhisit Vejjajiva,



Dr. Johan A. Aarli (front left) and Dr. Raad A. Shakir walk along the concourse of Government House in Bangkok.

as well as the governor of Bangkok, Sukhumbhand Paripatra, to discuss our concerns. We also visited the places where the protests had taken place, and everything seemed calm and was functioning normally.

There has been some uncertainty about the political situation in Thailand, and while there are occasional political demonstrations, they are usually peaceful and outside of government buildings. Daily and commercial life and activities such as conferences tend not to be disrupted. All delegates are of course advised to look at visa and travel advice from their national governments and ministries of foreign affairs before they travel.

Our Thai hosts have done everything possible to make this congress a success, and we look forward to see all of you in Bangkok in October. ■

Study Sheds Light on Features of Brain AVM Rupture

BY DOUG BRUNK
Elsevier Global Medical News

SAN DIEGO — Disabling neurological deficits caused by ruptured brain arteriovenous malformations seem to occur more frequently in malformations with exclusive deep venous drainage and in those that bleed into the brain parenchyma, results from a single-center study demonstrate.

"Hemorrhage is the most dangerous complication in the natural history of untreated arteriovenous malformations [AVMs] of the brain," Dr. Christian Stapf said at the International Stroke Conference. "We expected that AVM bleeding in eloquent locations would cause more functional damage to the brain, but we were unable to prove that in our study."

In an effort to determine the demographic, clinical, and morphological AVM characteristics associated with disabling neurological outcomes after acute AVM rupture, Dr. Stapf, of Columbia University, New York, U.S.A., and his colleagues studied 80 patients with an AVM who presented with intracranial hemorrhage at Hôpital Lariboisière in Paris, France, from 2003 to 2008. The

mean age of the patients was 40 years, 45% were women, and their median Rankin score was 2, with a range of 1–4.

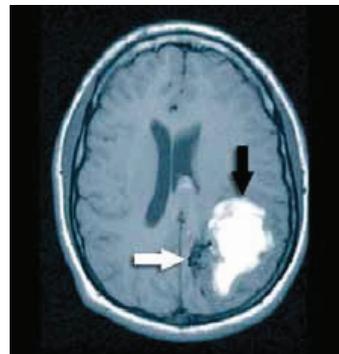
Dr. Stapf reported that of the 80 patients, 54 (68%) had intracerebral bleeding, 17 (21%) had a subarachnoid component and 29 (36%) had an intraventricular hemorrhage component, including overlapping bleeding locations in 20 cases. The mean AVM size was 20 mm, 67% were located in the lobar region of the brain, and 52% had a deep venous drainage pattern.

Retrospective studies cannot explain how bleeding may change the AVM's angiographic configuration.

DR. BUIS

meaning the ventricles or the subarachnoid space," Dr. Stapf said at the conference, which was sponsored by the American Heart Association. Dr. Stapf had no conflicts of interest in regard to the study, which was funded by the French ministry of health.

When the researchers compared the 48 patients with a median Rankin score of 2 or less (group 1) with the 32 patients with a median Rankin score of greater than 2 (group 2), the only statistically significant differences between them were parenchymatous location



An MRI shows hemorrhage of a brain AVM into the left parietal lobe (black arrow) and the AVM nidus (white).

(88% in group 1 vs. 54% in group 2) and a "deep only" venous drainage pattern (44% in group 1 vs. 21% in group 2).

"As a clinician, what should the consequence of this finding be?" Dr. Stapf asked. "If AVMs with exclusive deep venous drainage have higher spontaneous bleeding risk and unfavorable functional outcome after hemorrhage, should this be the target for preventive intervention before bleeding occurs? The bad side of that is that deep venous drainage is also associated with higher treatment risk as measured by traditional risk scores."

In an interview, Dr. Osvaldo Fustinoni noted that "if the treatment risks outweigh the benefits, treated patients

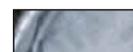
with unruptured AVMs are more likely to end up more severely handicapped" than if their unruptured AVM was left untreated.

Some evidence suggests that invasive treatment strategies are significantly associated with a more than threefold increased risk of AVM hemorrhage, and an increased risk of clinical impairment, said Dr. Fustinoni of the University of Buenos Aires.

Dr. Stapf noted that A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA), led by researchers at Columbia University, and supported by the U.S. National Institutes of Health and the National Institutes of Neurological Disorders and Stroke in Bethesda, Md., will shed light on further understanding of this complication. The trial is currently enrolling international sites to participate (www.arubastudy.org).

In an interview, Dr. Dennis R. Buis of VU University Medical Center, in Amsterdam, the Netherlands, said the ARUBA trial will increase the understanding of risk factors for bleeding from AVMs that have not previously bled because studies with a retrospective design, such as the current study, cannot account for how "bleeding may change the angiographic configuration of the AVM due to kinking of its vessels or compression on the AVM."

Neither Dr. Fustinoni nor Dr. Buis was involved in the study. ■



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Malawi's Radiological Advances Take Root

Before Westerners settled in central sub-Saharan Africa, medical subspecialties, especially those that were technology-based such as radiology, were virtually nonexistent. The resource-poor Malawi serves as an illustration of the emergence of radiology in this region.

There are 13 million people in Malawi, of which 87% live in rural areas. It is ranked in the bottom 10 countries on the United Nations Development Programme per capita income scale. Malaria, HIV, and respiratory and diarrheal diseases comprise the bulk of the disease burden, so preventive medicine is a health priority.

The development of radiology in Malawi follows the general trend of the growth of medical institutions in the country. The overall growth of medical services in Malawi falls into three periods: preindependence (pre-1964), postindependence (post-1964), and recent (the last 20 years). During the colonial era, medical services (and radiology) were concentrated in the cities of Blantyre, Zomba, and Lilongwe. Since British rule, the Queen Elizabeth Central Hospital (QECH) in Blantyre has been the largest medical facility in the country.

In the preindependence period, radiologic services consisted of plain radiography and limited use of oil-based contrast agents. General physicians interpreted the studies without assistance from specialists. QECH trained paramedical staff, including nurses and radiography assistants. There was no medical or radiography school. There were specialists in fields such as pediatrics, but not in radiology. Apart from chest and skeletal films,



BY SAM KAMPONDENI, M.B., CH.B., M.MED.

Dr. Kampondeni is chairman of the department of radiology at the Queen Elizabeth Central Hospital in Blantyre, Malawi.



BY MICHAEL POTCHEN, M.D.

Dr. Potchen is associate professor in the department of radiology at the University of Michigan, East Lansing, U.S.A.

the department performed selected contrast examinations, chief among them being myelography, cholecystography, hysterosalpingography, barium meal, and intravenous urography. Zomba and Lilongwe had similar radiology set-ups.

After independence from Britain in 1964, health services were expanded and better equipped hospitals were built in most of the country's districts. Each of the hospitals had an x-ray room and manual film-processing equipment, and the radiology department would be operated by a radiologic technologist. But the interpretation of the films remained in the hands of the general physician. The most common examinations were chest films for coughs and limb x-rays for trauma.

In the 1970s, QECH, Zomba, and Lilongwe hospitals were further improved to include ultrasound and angiography (at Lilongwe). QECH had a tomography x-ray unit. In the late 1970s, the Lilongwe

School of Health Sciences was established for training paramedical personnel, including radiologic technologists. It remains the country's only training institution for radiographers. It has produced over 100 radiographers, and the training has improved from basic training in radiography to the inclusion of ultrasound and CT skills.

Malawi has always been short of radiologists—only one or two have ever worked in the country at a time. Lilongwe Central Hospital had one radiologist from the late 1970s to the mid-1980s. From 2003 to 2004, the hospital was staffed by a German volunteer radiologist. Presently, there is one radiologist at QECH and two in training in South Africa and Kenya. There has been a single radiologist at QEHC since 1996. It remains a standard practice of clinicians with varying levels of expertise to request and read radiologic examinations.

Ultrasound examinations also are performed by clinicians.

Since 1998, radiology in Malawi has experienced accelerated growth. QECH, Zomba, and Lilongwe hospitals acquired improved x-ray units and automatic film processors. QECH acquired a Philips single-slice CT scanner in 1998. Around that time, the private hospitals of Mwaithu and Blantyre Adventist Hospitals also acquired CT scanners. These scanners altered the practice of medicine in the country. Their impact was particularly noticeable because they reduced referrals to South Africa for neurological diseases and sped up diagnosis of intracranial lesions, especially traumatic bleeds.

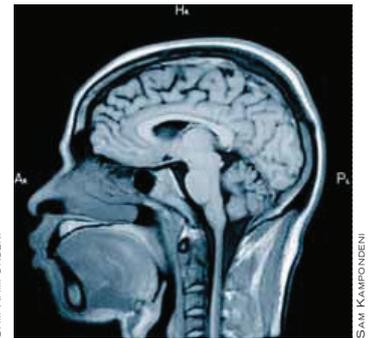
In 2008, Malawi opened its first MRI service, courtesy of the generous efforts of the Malawi Government, GE Healthcare, Michigan State University in the United States, and the U.S. National Institutes of Health. The service uses a 0.35T GE Signa Ovation scanner with the latest software technology. This is the country's only MRI scanner, and it serves patients from neighboring countries. It will provide imaging in neuroAIDS, skeletal trauma, orthopedics, and better imaging for children with cerebral malaria. It will also help in early detection and diagnosis of disease so patients need not leave the country.



Malawi acquired its first—and only—MRI machine in 2008. It is also used for patients from neighboring states.



This image of the lower lumbar spine was obtained at the new MRI service.



Patients need no longer leave Malawi for images such as this sagittal flair.

Neurological Pearl: Parsing Essential Tremor

BY ELAN D. LOUIS, M.D.

Essential tremor is one of the most common neurological disorders. To neurologists, the word “essential” may seem cryptic, but to patients, it is irksome, because it seems to suggest the disorder is in some way necessary. How did this word come to describe a condition that is anything but that?

Essential tremor was first used in 1874 by an Italian professor of medicine, Pietro Buresi, in describing a young man with severe, isolated action tremor. Buresi proposed the term *tremore semplice essenziale* (simple essential tremor). Notably absent from his report was a description of paralysis or other central nervous system signs.

Later, Edoardo Maraglio reported a 62-year-old man suffering from isolated action tremor. The patient's mother had also developed a generalized limb and trunk tremor at an advanced age. The tremor, which was severe and involved all limbs, had been noted soon after birth and worsened in adolescence and adulthood. However, aside from the tremor and mild gait unsteadiness, the neurological examination was normal.

Maraglio was apparently not aware of Buresi's work, as he did not cite the earlier publication. He proposed the term *tremore essenziale congenito* (essential congenital tremor). Several other seminal publications on this disorder followed in the early 1890s, including those of Anton Nagy and Fulgence Raymond.

Around the turn of the 19th century, the term began to appear more regularly in the literature. Authors noted characteristics that helped delineate it from other forms of tremor: it was hereditary and often multigenerational; it was the only symptom detected in patients; and it was present almost all the time.

In the 19th century, individual aspects of appearance, character, and health were viewed as highly resistant to change. A person was considered to be born with fixed features such as hair color, body form, and temperament, so that just as some people were thin and others had a fuller body, some had tremor and others did not. These were often viewed as simple, unitary properties, existing independently of other properties. These core elements of individuality were, in many respects, akin to physiologic constants. They were viewed as so firmly fixed

within the organized structure of the body that they were considered an intrinsic part of the individual makeup. Hence, the word “essential” seemed appropriate.

Although “essential” and “idiopathic” are conceptually similar, essential—which could be equated with familial or constitutional—diagnoses contrasted with idiopathic, which meant that the underlying cause was unknown. In this sense, the use of “essential” to describe the tremor embodied the notion of a constitutional property of an individual. The difference is subtle, but it provides an important clue as to how this emerging tremor disorder was viewed. Although the term has evolved in meaning over the last century, it has stuck, much to the chagrin of many confused E.T. patients.

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Dr. E. Broussolle, Dr. C.G. Goetz, Dr. P. Krack, Dr. P. Kaufmann, and Dr. P. Mazzoni contributed to this and an earlier article on this topic (*Neurology* 2008;71:856-9).



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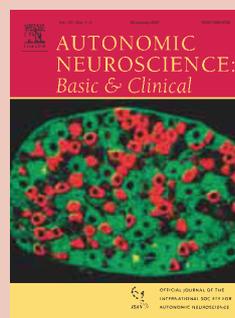
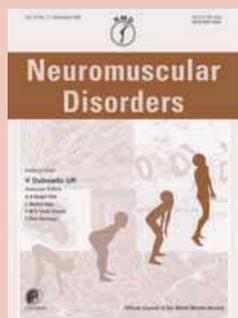
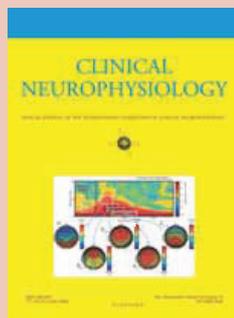
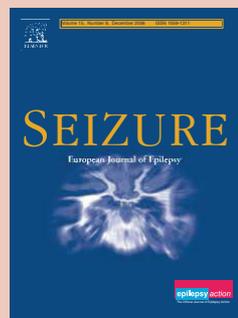
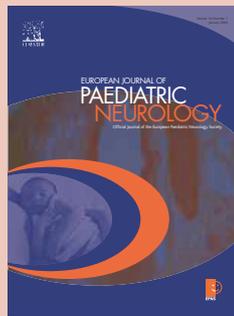
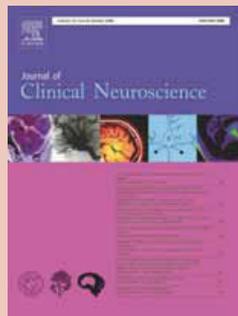


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OBITUARY

Daniel Carleton Gajdusek (1923-2008)

BY LEV G. GOLDFARB, M.D.

Daniel Carleton Gajdusek, who died on Dec. 12, 2008, at age 85, was an active contributor to the fields of neurovirology and neurogenetics. He received his highest recognition in 1976, when he won the Nobel Prize for Medicine for the discovery of a new class of infectious agents, later named prions. His work outlined a group of neurodegenerative disorders known as spongiform encephalopathies, which include kuru, Creutzfeldt-Jakob disease, fatal familial insomnia, and several other disorders shown to be transmissible.

Dr. Gajdusek was born in 1923, in Yonkers, New York, U.S.A., into a family of immigrants from Slovakia and Hungary. He attended the University of Rochester in New York, then Harvard Medical School in Boston, Mass., U.S.A., and spent several postdoctoral years first at Harvard and later at the California Institute of Technology in Pasadena, U.S.A., where he worked with Nobel laureates Linus Pauling and Max Delbrück.

During his military service at the Walter Reed Army Medical School in Washington D.C., U.S.A., he was sent to post-war Germany on a mission to save orphaned children. He later travelled to Iran, Afghanistan, and Turkey and subsequently to Bolivia, Amazonia, and Peru to collect data on epidemics of rabies, plague, and arbovirus infections. On these trips, he became increasingly fascinated with rare diseases in little-known, remote world populations.

He had trained as a pediatrician and neurologist at Harvard and started a program on child growth and development and disease patterns in remote cultures, which he later continued at the U.S. National Institutes of Health (NIH) in Bethesda, Maryland.

In 1955, Dr. Gajdusek worked temporarily at the Burnet Institute in Mel-



Carleton Gajdusek tracked and studied disease patterns in remote cultures.

bourne, Australia, where the research focus is infectious diseases. While he was there, he visited tropical Australian tribes and subsequently went to New Guinea, where he discovered a previously unknown deadly disease that locals called kuru. He set up systematic studies of disease, built a hospital for kuru patients, and spent months in the field documenting each of several thousand cases of the disease and performing autopsies.

Kuru had emerged in the early 1900s in a small indigenous population of the New Guinean Eastern Highlands and reached epidemic proportions in the mid-1950s. It is a subacute neurodegenerative disease presenting with limb ataxia, dysarthria, and shivering tremor. Speech deteriorates as the disease advances. Dystonic movements and myoclonus-type jerks are present in the trunk, limbs, neck, and jaw. Dementia may not be evident until later stages of illness. The disease progresses to complete motor and mental incapacity and death within 6 to 24 months. Kuru neuropathology is represented by severe neuronal loss, spongiform change, astrocytic and microglial proliferation,

highly characteristic ("kuru-type") amyloid plaques, and prion protein deposits in the cerebral cortex and cerebellum. Astrocytic proliferation and astrogliosis are widespread and intense, but no inflammatory changes are observed. The disease was prevalent in women and children, but rare in adult males.

During a 1959 visit to Dr. Gajdusek's laboratory at the NIH, veterinary neuropathologist James R.M. Innes noted similarities between neuropathology findings in kuru and scrapie of sheep, a slow viral infection in which susceptibility is genetically determined. Another veterinarian neuropathologist, William J. Hadlow, also suggested in a letter to the *Lancet* a possible relationship between kuru and scrapie and recommended that the transmissibility of kuru be tested in laboratory primates. These suggestions stimulated the ongoing attempts to find a microbial etiologic agent.

In 1966, Dr. Gajdusek, C.J. Gibbs, and M. Alpers reported the transmission of kuru to chimpanzees (*Nature* 1966;209:794-6). Follow-up studies showed kuru agent is uniquely resistant to physical and chemical treatments that would otherwise destroy "conventional" viruses. The higher prevalence in women and children, was explained by their preferential participation in cannibalistic funeral rituals, during which brain tissue of kuru victims was consumed or rubbed into children's skin.

The fact that a neurodegenerative disease such as kuru was caused by an infectious agent prompted the analysis of several other progressive neurodegenerative disorders. The interest first focused on Creutzfeldt-Jakob disease (CJD). In 1968, Dr. Gajdusek and his coinvestigators reported that an infectious agent similar to kuru was transmitted to chimpanzees from CJD brains after a 12-month incubation (*Science* 1968;161:388-9). The findings that purely neurodegenerative diseases had an infectious origin and the

subsequently described cases, were completely new and unexpected.

The latest member of this group, variant Creutzfeldt-Jakob disease that is linked to the transmission of bovine spongiform encephalopathy (mad cow disease) to humans, shows features similar to kuru.

Several unrelated neurological disorders have been successfully investigated at Dr. Gajdusek's NIH laboratory: tropical spastic paraparesis, amyotrophic lateral sclerosis/parkinsonism dementia complex of Guam, characterization of spinocerebellar ataxia genes, and the discovery of the amyloid precursor protein gene playing a critical role in Alzheimer's disease.

Dr. Gajdusek's interests spanned classic literature, music, the fine arts, history, ethnography, and human development. He was a warm and kind man. He gave his staff and students complete freedom and encouragement. Over the years, he took 48 orphaned teenagers from New Guinea and Western Pacific region back the United States. He adopted them and educated them; some subsequently returned to their homeland to offer services at the highest levels of government and society.

Having worked closely with Dr. Gajdusek for almost 30 years, I remember his exceptional qualities—the clarity, speed, and depth of his thinking, his attention to detail, and his ability to organize and direct his thinking.

He made lengthy daily entries in his diaries, using a typewriter he carried with him, or in later years, dictating into a tape recorder. The public has inherited his published books, more than 1,000 research papers, and the multivolume set of notes of a passionate and productive scientist, thinker, and generous human being. ■

DR. GOLDFARB is the head of the Clinical Neurogenetics Unit at the National Institute of Neurological Disorders at the NIH in Bethesda, Md., U.S.A.

Charting the Course of the World Neurology Foundation

The World Neurology Foundation was incorporated in 1999 as an independent nonprofit organization to serve as a charitable arm of the World Federation of Neurology in the United States of America. (WFN is a registered charity in the United Kingdom.)

Dr. James Toole, a former WFN President, conceived of the idea to allow for tax-deductible donations to be made in the United States to help fund the WFN's international projects. Canadian donors benefited because of the tax treaties between the two countries.

Under the presidencies of Dr. Toole and Dr. Antonio Culebras, the foundation secured funding for four endowed lectureships to be presented at the World Congress of Neurology in Bangkok honoring Dr. Bhim Singhal (India), Dr. Eddy Bharucha and his wife, Dr. Pilo

Barucha (India), Dr. Melvin Yahr (U.S.), and Dr. Richard Masland and his wife, Dr. Mary Masland (U.S.). This support will continue for the biennial congresses.

Since 2005, the foundation has accepted responsibilities in two new areas. The first initiative is based on data in the 2004 Atlas of Country Resources for Neurological Disorders by the WHO and WFN, which showed a global need for better neurological services, especially in Africa.

On assuming the WFN presidency, Dr. Johan A. Aarli recognized those needs and committed resources to improving the services. He included the federation in the coalition of organizations that have worked on the Africa Project. As president of the foundation and together with an able board of directors, I have supported this new initiative.

African neurologists requested basic tools for the neu-

rological exam. In response, the foundation conceived of the Neurologist's Tool Kit, consisting of a 128-Hz tuning fork, a stethoscope, a collapsible Queen Square reflex hammer, a pen light, an NIH stroke scale, and a Snellen chart, stored in a portable case. Last year, 100 kits were distributed at meetings in Senegal and Cameroon and to Zambian trainees. The foundation is seeking funding for kits for neurologists in Uganda, Ethiopia, and Nigeria.

The second initiative grew out of the success of the American Academy of Neurology's Palatucci Advocacy Leadership Forum, which trains three international advocates a year, each of whom devises a project to improve neurologic services in their home countries. The foundation has helped these individuals formulate the projects and find funding. Members of the Pakistan International Neuroscience Society and of the Association of Indian Neurologists in America have contributed to active projects.

For more information about the foundation or to make a donation, visit www.worldneurology.org. ■



BY MICHAEL FINKEL, M.D.

Dr. Finkel is a neurologist who is in private practice in Naples, Fla., in the United States.



BOOKS TO CONSIDER

Resource Update

Myasthenia Gravis and Related Disorders, edited by Henry J. Kaminski (New York: Humana Press, 2009)

The editor and contributors to this new edition have approached the difficult task of providing an overview of the complex disease myasthenia gravis. Many chapters are written by international experts who have made pivotal contributions to the field, and as such, the book provides an integrative view of this disease and related disorders.

Most of the illustrations are of excellent quality, especially those representing neurophysiologic and molecular mechanisms. Some of the color plates could just as easily have been shown as black and white figures. Immunology chapters are excellent, especially those referring to T-cell education in thymomas.

Given the substantial progress in understanding the pathophysiology of myasthenia gravis, a more detailed discussion or perhaps a separate chapter on specific clinical aspects and therapy of MuSK-myasthenia, which poses a number of therapeutic challenges, would have been desirable. The same pertains to management of malignant thymomas.

What improvements could be made? More discussion about the systematic introduction into clinical monitoring of disease via scoring (Besinger-Toyka score) and escalating therapy algorithms in severe cases would have been helpful. As with multiple sclerosis, baseline therapeutics and individualized trials with combination therapies or monoclonal antibodies can be envisioned for MG.

Treatment of MG in the intensive care unit has become rare: less than 2% of pa-

tients have a disease crisis in their lifetime. The threshold of a forced vital capacity less than 1 L only pertains to extremely slow deterioration; especially in rapid progression, vital risks may start when FVC reaches 1.5 L. Soft warning signs such as weakness of neck extensor muscles, and fluctuating swallowing and respiration should be mentioned.

The application of BiPAP to bridge respiratory symptoms has been significant progress in ventilatory management. When plasma exchange proce-



BY RALF GOLD, M.D.

Dr. Gold is professor and chair of the department of neurology at Ruhr University Bochum in Germany.

dures have to be considered in MG crisis, immunoadsorption via tryptophan columns should be mentioned as well.

In accord with the personal approach noted by Dr. Kaminski, I will also make some personal comments. The title picture may be slightly misleading, since associated gynecomastia rather points to nonrelated medical conditions or Kennedy syndrome. Having studied with the late Dr. Hertel Mertens, I would like to see an acknowledgement of his introduction of azathioprine mentioned with the reference to the 1981 paper in the *Annals of the N.Y. Academy of Sciences*. The disorder is often associated with Mertens and Isaacs, who described neuromyotonia almost simultaneously. ■

New Look at Old Physicians

Old Endeavour: Scientific and Humanitarian Contributions by Physicians Over Age 65, by William C. Gibson. (International Association for Humanitarian Medicine Brock Chisholm, 2007)

In an earlier work, Dr. William Gibson, a neurologist and medical historian, documented the contributions of medical undergraduates to the field. It is an equal pleasure to read his latest offering, in which he outlines 129 physicians who made contributions after age 65, some extending their life's work into a ripe old age and others moving to entirely new areas.

One of my favorite stories has always been that of Dr. Peter Mark Roget, whose retirement project was to collect words into a thesaurus. His notable career change in the twilight of his life has mostly been forgotten, but I'm sure every one of us has some or other version of his thesaurus close at hand.

Or take Santiago Ramón y Cajal, who published *Degeneration and Regeneration in the Nervous System* at age 76, and *Neuronismo o Reticularismo* at age 83. Sir Charles Sherrington clearly followed Cajal's example, writing an introduction to Cajal's biography at age 92.

Sir John Eccles published three major books on the nervous system between ages 65 and 80, and his last publication appeared after his death at age 95. Neurosurgeon William Feindel, still active at the Montreal Neurological Institute at age 90, has published 258 papers singly or with colleagues since his "retirement," almost as many as he published before his 65th birthday. Then there are neuro-

scientists Edith and Patrick McGeer, now in their 80s, who maintain active laboratories and have published 175 manuscripts since official retirement and "hope to contribute 200 more."

Readers can undoubtedly add their own examples from personal experiences. I remember visiting with Macdonald Critchley as he was sending his biography of Hughlings Jackson to the publisher shortly before he died at 97.

Of course, Dr. Gibson himself is an excellent example of the senior scholarly physician who "keeps on ticking."



BY T. JOCK MURRAY, M.D.

Dr. Murray is a professor emeritus at Dalhousie University, Halifax, N.S., Canada. To purchase the book, e-mail contact@iahm.org.

Now in his ninth decade, he has had a remarkable career as a neurologist, neurophysiologist, researcher, teacher, author, medical historian, bibliophile, musician, and philanthropist.

He was a founder of the American Osler Society, chancellor of the University of Victoria, warden of Green College, Oxford, and a vital figure in the establishment of a number of major academic institutions.

In an age of physician burnout and early (or mandatory) retirement, it is reassuring to know there are professionals who ignore arbitrary age classifications and keep on contributing—especially as more of us approach that age. ■

FROM THE JOURNAL OF THE NEUROLOGICAL SCIENCES

AMM and Diabetic Polyneuropathy

Many systemic diseases are known to affect peripheral nerves diffusely. The most common is diabetes mellitus, but there are many other causes of different classes of disease. Such examples would include metabolic problems such as uremia, toxic neuropathy from alcohol or medications, nutritional conditions due to thiamine and vitamin B₁₂ deficiency, and infections such as HIV disease.

In each case, although the association between the systemic disease and polyneuropathy is well known, there is a dearth of detailed data to characterize the pathogenesis. Clearly, these are sick neurons; their fragility leaves them vulnerable to the effects of pressure, and these patients are commonly affected by carpal tunnel syndrome, ulnar and peroneal neuropathy, or other pressure-related neuropathies.

A fruitful approach to investigating this problem would be to identify at-risk patients with mild asymp-



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

Dr. Tselis is an associate professor of neurology at Wayne State University, in Detroit, Michigan, U.S.A. He is the book review editor for the Journal of the Neurological Sciences.

tomatic disease and study them in detail. In that way, a cohort of patients with diabetic polyneuropathy (DPN) could be evaluated for a pressure neuropathy to which they are especially susceptible. Such a cohort can be divided into those with and those without a pressure palsy, and the two groups could be compared.

The study, reported in a paper by Dr. Eleftherios Stamboulis and colleagues, illustrates one of the first steps in this type of strategy (*J. Neurol. Sci.* 2009;278:41-3). Dr. Stamboulis, who has been investigating diabetic neuropathy for 30 years, and his team recruited 100 diabetes patients who were participating in a clinical trial and had electrodiagnostic diagnosis of an asymptomatic median mononeuropathy (AMM) of the non-dominant arm. They were classified into four grades of DPN and according to the presence or absence of AMM.

The analysis of these patients was instructive. The researchers found that AMM was present in 28% of these patients overall. It was significantly more common in those with more severe DPN, but it did not depend on the duration or nature (type 1 or type 2) of diabetes.

However, there were some unexpected results. Some patients with mild DPN had AMM (18% of those with stage 0 DPN), and some with severe DPN were free of AMM (55% of those with stage 3).

These results, if robust, have pathogenetic implications. Thus, although DPN is likely a result of relative tissue ischemia, proportional to the total exposure to hyperglycemia, other factors contribute to the fragility, given that some patients had unexpected AMM and others did not. This implies that other factors contribute to the risk and severity of disease. One possibility is that of mitochondrial involvement (as is likely the case for the neurotoxic effects of certain antiretroviral drugs).

These results will need replication, but they clearly signal that multiple factors affect the diabetic nerve. Further research will be needed to characterize these factors and allow the design of specifically targeted therapy. ■

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