VOL. 27 • NO. 2 • APRIL 2012

WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

# Plan Addresses Epilepsy in Latin America

BY JEFF EVANS
*Elsevier Global Medical News*

Last year, member nations of the Pan American Health Organization endorsed a strategy and action plan on epilepsy that seeks to improve the identification, treatment, and human rights of people with epilepsy.

It is the first time that the Pan American Health Organization (PAHO) – the oldest regional health organization in the world – approved a neurological program as a priority, according to Dr. Marco T. Medina, who is the World Federation of Neurology's newly elected regional director for Latin America.

"This is one of the most important examples of what a region can do together for a neurological problem, because this is the first time regionally that a neurological problem has been put in the agenda of the governments as a priority," Dr. Medina said in an interview.

The impetus for the strategy and action plan derives from a number of earlier resolutions and programs from the World Health Organization (WHO) and the PAHO, including the 1997 Global Campaign Against Epilepsy, the 2000 Declaration of Santiago on Epilepsy in Latin America, and the WHO's 2008 Mental Health Gap Action Program, which recognized epilepsy as one of eight priority conditions.

The strategy and action plan is sorely needed. In the Americas, about 5 million people have epilepsy, but it is estimated that more than half of those with epilepsy in Latin America and the Caribbean have no access to services, according to the WHO.

The International League Against Epilepsy (ILAE) appointed Dr. Medina; Dr. Jorge Rodriguez, chief of PAHO Mental Health; and

*See* **Epilepsy** • *page 8*

COURTESY HONDURAS NEUROLOGY TRAINING PROGRAM, UNAH

**A patient receives an EEG evaluation for epilepsy as part of the first phase of the Honduras Treatment Gap Project in the city of Juticalpa.**

## INSIDE



# Knowledge of New Mutation in ALS, Dementia Grows

BY BECKY McCALL
*Elsevier Global Medical News*

In recent months, the discovery of the C9ORF72 mutation has added fresh insight into the causes of frontotemporal dementia and amyotrophic lateral sclerosis, and now a series of new studies describes the frequency of the mutation and how the mutation reveals itself clinically in a spectrum of phenotypes in patients with either disease.

The series of studies found that the mutation most often is associated with behavioral variant frontotemporal dementia (FTD), and occurred in 2%-5% of patients with sporadic FTD and 15%-48% of patients with familial FTD. For amyotrophic lateral sclerosis (ALS) patients, the mutation occurred in 4%-7% of sporadic cases and 22%-43% of familial cases. Another 20%-40% of patients who show symptoms of both diseases had the mutation; the rate reached almost 50% among these patients with a family history of ALS or FTD. Some studies reported finding the mutation in 0%-28% of patients who present with the progressive nonfluent aphasia variant of FTD.

The eventual clinical impact of identifying the C9ORF72 mutation is the availability of a population of at-risk carriers of the mutation to aid research into the preclinical phase of disease, said Dr. Kevin Talbot, professor of motor neuron biology at the University of Oxford, England. "Rather than work in the phase of established disease, which may be intractable to disease-modifying therapy, this provides a new departure to 'fill in' a phase in the natural history of ALS which has hitherto not been amenable to study." Dr. Talbot was a coauthor on a study that screened 4,448 patients with ALS and 1,425 patients with FTD for the mutation (Lancet Neurol. 2012 March

*See* **Mutation** • *page 14*

## In This Issue of World Neurology

## EDITOR IN CHIEF'S COLUMN

MARK HALLETT, MD

# New Leadership to Continue WFN Mission

With this issue, I end my 4-year term as editor in chief of World Neurology. It has been both fun and educational to take a very broad view of the activities of our profession.

Generally, neurological problems are the same around the world, except for the increased incidence of various infections in Africa, India, and various parts of South America. The infections have been highlighted because every neurologist needs to know about them; with increased mobility any infection might show up anywhere.

However, there is also epilepsy, stroke, and neurodegenerative disease. Here we need to educate doctors and health care workers to bring modern medicine to patients everywhere. An interesting trend that will help in this regard is telemedicine. The WFN is our professional organization and it builds links between the world's neurologists. It can help tackle the world's problems, but it needs the help of everyone.

World Neurology, this newsletter, can play a role in bringing news of all these concerns and the Federation's activities to every neurologist. In my tenure, the size and scope of World Neurology increased to report on more information about the WFN and provide more neurology news. The feedback that I have received is that this effort has been successful.

However, two factors are at play to change the format yet again. One is that the current format is expensive, and, two, is that electronic media are getting more popular and widely available. Looking forward, World Neurology may well become all electronic.

There are many persons to thank. Renée Matthews was my managing editor from the International Medical News Group (IMNG) most of the time. She was assisted by Jeff Evans, who now will take over the operation. They have been great. The editorial board has been helpful, particularly Alex Tselis, the liaison to the Journal of Neurological Sciences, who contributes articles to the newsletter, and Michael Finkel, who is always full of good ideas and has lots of contacts around the world. The officers of the WFN – Dr. Vladimir Hachinski, Dr. Raad Shakir, and our executive director, Keith Newton – have been supportive and helpful.

Past President, Dr. Johan Aarli, hired me for this job and was very helpful as I began. He is now taking over the position of editor in chief of World Neurology going forward. I cannot think of a better choice, and I wish him good times. Most important, I have to thank all those neurologists around the world who have contributed articles. It is the newsletter of all the world's neurologists and Johan Aarli will be counting on your continuing help. ■

## Nominating Committee Recommendations for the 2012 Election

The nominating committee of the World Federation of Neurology has recommended the following candidates for the elected trustee post that will become vacant on Sept. 9, 2012, at the Annual General Meeting of the Council of Delegates:

- Prof. Wolfgang Grisold (Austria)
- Dr. Raul Federico Pelli-Noble (Argentina)
- Prof. Jean Schoenen (Belgium)

Anyone can make additional nominations by obtaining the supporting signatures of five or more authorized delegates and submitting the name(s) of the individual(s) in question to the Secretary-Treasurer General, in care of the London Secretariat office.

The nominations need to arrive at least 30 days prior to the date of the Council of Delegates meeting. ■

**Visit the World Federation of Neurology's newly redesigned Web site at www.wfneurology.org. You can download current and past issues of World Neurology.**



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 IMNG Medical Newswire.



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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.



IMNG MEDICAL MEDIA

**Global Medical Research**
**Publisher** Peter F. Bakker

**Elsevier Global Medical News**
**A Division of IMNG Medical Media**
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## PRESIDENT'S COLUMN

VLADIMIR HACHINSKI, MD

# The Formation of the Latin American Federation Of Neurological Societies

The development of a Latin American Federation of Neurological Societies was launched during the 13th Pan American Congress of Neurology in La Paz, Bolivia, held March 4-8. This follows the Marrakesh Proclamation for the formation of such a Federation during the World Congress of Neurology in Marrakesh, Morocco, Nov. 12-17, 2011. This was initiated by Gustavo Roman and Ana Robles, the outgoing Regional Director for Latin America, and representatives from the Latin American countries: Juan Carlos Duran (Bolivia), Francisco Cardoso (Brazil), Sergio Castillo (Chile), Jesus Rodriguez (Colombia), Dennis Chinchilla (Costa Rica), Ana M. Robles (Dominican Republic), Oscar Del Brutto (Ecuador), Marco Tulio Medina (Honduras), Ricardo Rangel Guerra (Mexico), Fernando Gracia (Panama), Alejandro Scaramelli (Uruguay), and Santiago Fontiveros (Venezuela).

The World Federation of Neurology (WFN) offered to consider providing through its grants program resources to create an infrastructure for the new Federation until such a time as a more permanent source of income can be obtained. In part to support the new Federation, and in part because having more frequent Congresses of Neurology will foster neurology in more regions, the delegates decided to move the Pan American Congresses from a 4-year cycle to a 2-year cycle in partnership with the WFN, the host society, and the newly formed Pan American Federation of Neurological Societies. The delegates of Brazil, Mexico, Panama, Paraguay, Puerto Rico, and Venezuela have expressed interest in hosting the Pan American Congress of Neurology. For practical reasons, moving from a 4- to a 2-year cycle will not be feasible until after the next Pan American Congress of Neurology to be held in 2016.

COURTESY DR. VLADIMIR HACHINSKI

**Puerta del Sol (The Sun's Gate) is symbolic of the highly sophisticated culture that thrived in the area of Bolivia and surrounding countries between 700 and 1200 AD.**

In line with a new democratic spirit within the WFN, it was decided that the new Regional Director would not be appointed, but be elected. Carlos Ketzoian (Uruguay) suggested a list of desirable attributes of such an individual, a description complemented by further suggestions by the delegates. Candidates were invited to participate in the election, provided that they were nominated by a minimum of two delegates from participating countries. Two candidates emerged, Marco Tulio Medina from Honduras and Ricardo Allegri from Argentina. Both were invited to present their vision to the delegates, followed by questions. After each had an opportunity of stating his proposals and answering the questions of the delegates, a secret vote was held and Marco Tulio Medina was voted the new Regional Director for Latin America. Ricardo Allegri will serve as a Vice President of the WFN Applied Research Committee.

The main task of the new Regional Director is to develop a structure for the new Federation in preparation of the democratic election of Officers in 2 years. He will be aided by the Commission headed by Ana Robles that will develop a constitution and bylaws, and by the Pan American Congress of Neurology Congress Committee that will include Juan Carlos Duran, organizer of the 13th Pan American Congress.

The leaders of WFN activities in the Americas will be Gustavo Roman, Chair of the Latin America Initiative; Ricardo Nitrini (Brazil), Vice Chair; and Marco Tulio Medina, ex officio Vice President as Regional Director. Their duties will include coordinating educational programs in Latin America in collaboration with the WFN.

May the sun shine upon the newly formed Latin American Federation of Neurological Societies! ■

## MEETING REPORT

# Bringing Neurology to Pan American Primary Care

BY SILVIA KOCHEN, MD

The number of neurologists in Bolivia is much lower than the rate per capita recommended by the World Health Organization, and so it is essential to provide the basic tools for the diagnosis and treatment of neurological disorders to primary care physicians and family doctors.

For that reason, a conference was held during the 13th Pan American Congress of Neurology in La Paz, Bolivia, March 4-8, 2012. It featured focused training on basic concepts of methodology and epidemiology and on the most frequent neurological diseases such as stroke, epilepsy, dementia, headache, and central nervous system infections. The conference was sponsored by the World Federation of Neurology, the Pan American Society of Neuroepidemiology, and the International League Against Epilepsy's Latin American Commission.

The conference was organized as a classroom course with free but compulsory registration and a total of 20 hours of teaching, divided into 4 hours per day. In agreement with the health authorities of Bolivia, each authorized participant who had complete attendance in the course received a legal certificate to place in their training curriculum. Each participant also received a CD with all the materials presented in each class.

**TRAINING FOCUSED ON BASIC CONCEPTS OF METHODOLOGY AND EPIDEMIOLOGY AND THE MOST FREQUENT NEUROLOGICAL DISEASES.**

A total of 350 people enrolled for the course, but admission had to be declined to about 100 applicants because of a lack of space in the physical location of the event. The students' daily presence and their interest and active participation in the seminars were remarkable.

In the last hour of the final day of the course, we asked all participants to give their thoughts about the conference anonymously. There was a very positive outlook, and the initiative was highly valued among the attendees. They said that they had never before been asked to participate in a similar activity. They emphasized the importance of the information received and noted the lack of taboos with many of the concepts seen during the course to eliminate the fear of seeing patients with neurological diseases. They identified not only the difficulty in diagnosis but also in monitoring these patients. They were highly likely to implement what they had learned into their daily practice. They emphasized the importance of diagnostic and treatment protocols, as well as the educational value of reviewing "clinical cases." Some criticized the lack of teaching materials before the conference and requested the repetition of similar activities.

We considered this course to be a valuable experience. It demonstrated that it is essential to consider the importance of providing knowledge about the care of neurological disorders to primary care physicians in developing countries. We suggest repeating this experience in other countries, and attracting an audience of general practitioners by inviting leading neurology specialists in each congress of neurology. ■

DR. KOCHEN *is the epilepsy section head in the division of neurology at Hospital "R. Mejia," a researcher at CONICET (National Council for Scientific and Technical Research), a professor of neurology at the University of Buenos Aires, and the Education Secretary of the Latin American Commission of the International League Against Epilepsy.*

FROM THE WFN HISTORY GROUP

# Over the Seas: Three 19th-Century Australia Neurologists

BY MERVYN J. EADIE, AO, MD, PHD

During the final two decades of the 19th century three Australian men, born within a decade of one another, undertook the long sea voyage from Sydney to Britain to further their medical and neurological experience. Their subsequent careers followed rather different courses that manifest different patterns of interchange between the neurologies of Europe and the antipodes. They were pioneers of a career pattern that many Australian neurologists and neuroscientists followed during the 20th century while Australian neurology matured and increasingly became educationally self-sufficient.

The first-generation Australians George Edward Rennie (1861-1923), Alfred Walter Campbell (1868-1937), and Grafton Elliot Smith (1871-1937) were all educated in New South Wales to the stage of university entry.

Courtesy Mrs. V. Hope

**Alfred Walter Campbell**

Rennie, who was born in Sydney, took a BA degree from the University of Sydney because no Australian university medical course was available at the time and then sailed to London in 1883. He graduated with an MB in 1887 and with an MD a year later. After returning to Sydney, he worked as a physician and pathologist. In 1898, he again sailed to London, acquiring further neurological knowledge at Queen Square and qualification as a member of the Royal College of Physicians. Returning to Sydney, he achieved a considerable local reputation as a physician with major neurological interests, publishing some neurological case reports and review-type articles. However, his career had little international neurological impact.

Campbell was born on a pastoral property near present-day Canberra. Although he was young enough to enter the new Sydney University medical course, he sailed to Britain in 1886 and graduated MB ChM (Edinburgh) in 1889. He spent 2 years gaining experience at Queen Square, in various British mental asylums, in Prague, and in Vienna with Baron Richard von Krafft-Ebing. His thesis, "The pathology of alcoholic insanity," brought him an Edinburgh MD.

For 13 years, Campbell was medical officer and pathologist to the Rainhill Asylum in Liverpool, England. In that time, he published a substantial number of major neuropathological studies. These included his collaboration with Henry Head on the famous investigation of the pathology of herpes zoster that defined the distribution of the dermatomes and his great monograph of 1905, "Histological Studies of the Localisation of Cerebral Function," which provided the first detailed account of the cytoarchitectonics of the primate and human cerebral cortex.

Campbell later returned to Australia after an absence of nearly 20 years. He spent the remainder of his life in Sydney practicing clinical neurology. Others had preempted him for appointments in neuropathology and psychological medicine. Campbell published further neuropathological and neurohistological studies of originality and merit, but his career in Australia, distinguished enough though it was, did not fulfil his earlier outstanding promise. He had been away from his homeland for too long before returning.

Smith was born in the provincial town of Grafton. He undertook the Sydney medical course and then spent several years carrying out neuroanatomical studies in that University's anatomy department, gaining an MD.

With a scholarship, he sailed from Sydney to Britain, subsequently doing further research in the Cambridge anatomy department before occupying, successively, chairs of anatomy at Cairo, Egypt; Manchester, England; and University College, London. During his career, he was responsible for a great deal of anthropological, neuroanatomical, and paleopathological research, and collaborated with Dr. William H.R. Rivers in work on psychological trauma.

Smith also was involved in the Piltdown man affair. He was one of several authorities who accepted that a skull and jawbone found in 1912 in a gravel pit in East Sussex, England, were fossil remains of a hitherto unrecognized human ancestor; 40 years later they were proved to be part of a deliberate hoax. Nonetheless, Smith proved to be a very considerable figure in the Egyptology, anthropology, and neuroanatomy of his time, a fellow of the Royal Society, and a knight. On two occasions, in 1914 and 1924, he returned to Australia for visits, but never again lived in his homeland.

Most Australian neurologists in at least the first two-thirds of the 20th century tended to follow training and career patterns resembling that of Rennie. A few resembled Smith's, and even fewer, Campbell's. Few attained such great international scientific distinction as Campbell or Smith. ■

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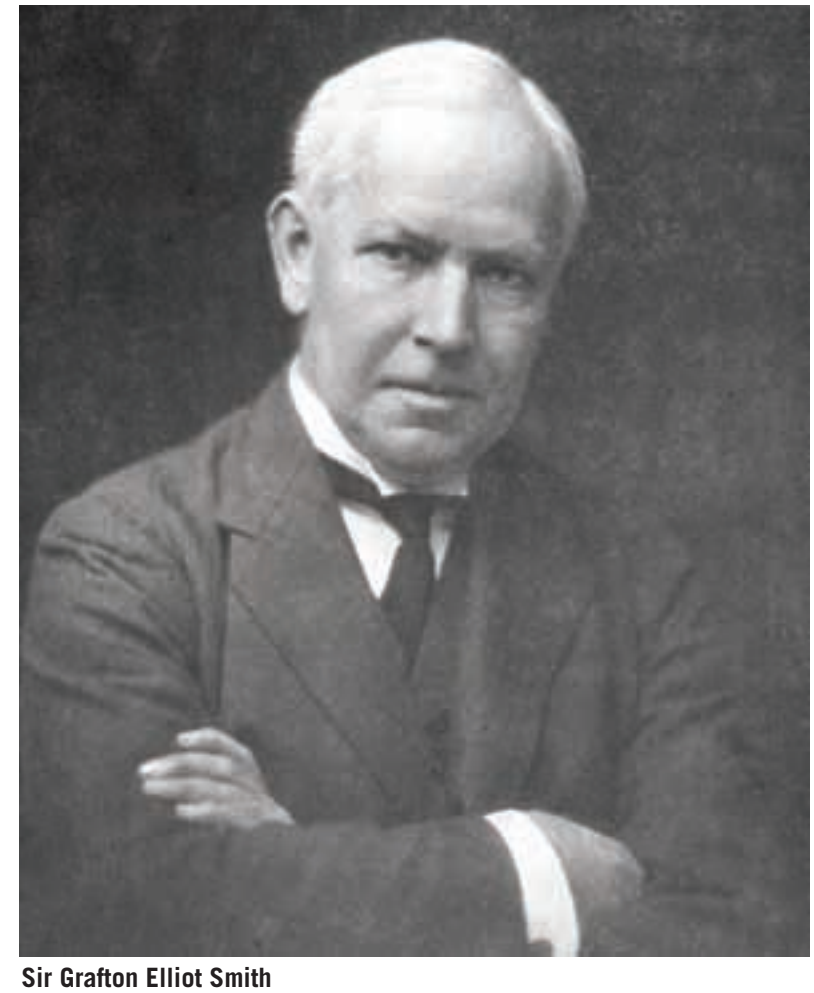
**George Edward Rennie**

*Dr. Eadie is emeritus professor of clinical neurology and neuropharmacology at the University of Queensland and honorary consultant neurologist at the Royal Brisbane and Women's Hospital, both in Brisbane, Australia.*



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**Sir Grafton Elliot Smith**

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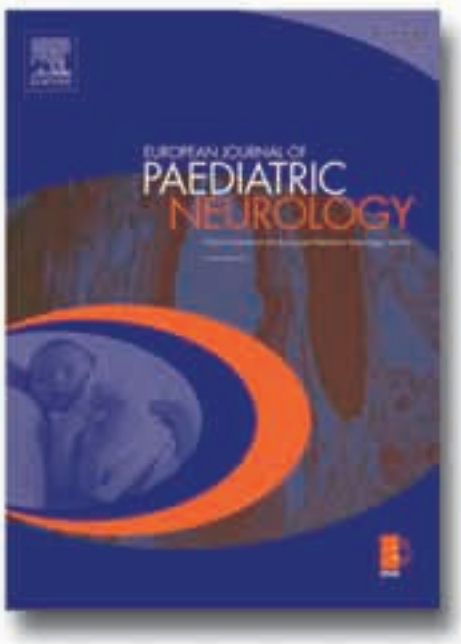


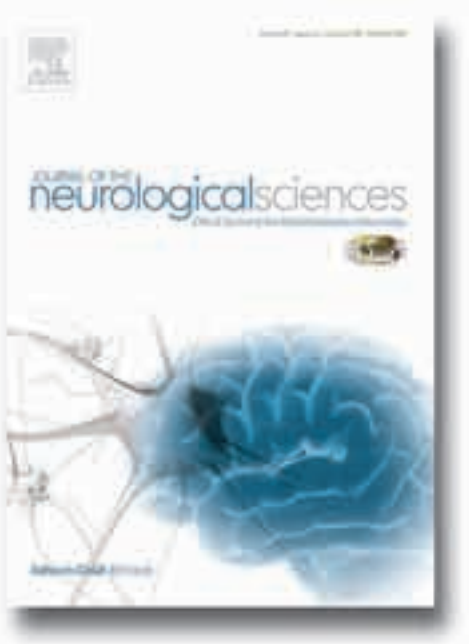


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NEUROLOGY

# Working Group Is Interconnecting Young Neurologists Worldwide

BY WALTER STRUHAL, MD

Representatives from many regions within the World Federation of Neurology have become members of the International Working Group of Young Neurologists and Trainees since its formation in 2009 and its inaugural meeting at the World Congress of Neurology in Bangkok, Thailand. The IWGYNT's vision is to advocate for the interests of young neurologists on a worldwide basis within the World Federation of Neurology (WFN). We are proud that we have one member elected to represent our group within the WFN's Education Committee.

Our mission is to:

- ► Represent the interests and initiatives of residents and young neurologists with a single voice.
- ► Establish networking among young neurologists.
- ► Support international training exchange.

The group is organized as a panel consisting of two delegates from each continent. Delegates may be sent only by a national or international neurological body representing young neurologists in that area. Currently Africa, Asia, Europe, and Australia and New Zealand have sent delegates to the IWGYNT. In the first 2 years of our existence, we have focused on establishing a network among young neurologists in the continents we are representing.


PHOTOS COURTESY DR. WALTER STRUHAL

**IWGYNT neurologists Walter Struhal, Xenia Kobeleva, Johann Sellner attend WCN 2011.**

### Africa

Our two delegates from the Pan African Association of Neurological Sciences, Dr. Rufus Akinyemi and Dr. Faustin Yepnjio, actively promoted the IWGYNT in many African meetings. They established a database of young African neurologists and interconnected them, which led to a tremendous improvement of organization within young African neurologists.

### Asia

Our delegate from the Association of South East Asian Nations Neurological Association, Dr. Surat Tanprawate, was extremely active in promoting the IWGYNT at Asian meetings and administrating the Facebook page of the IWGYNT. He has established a working network of young Asian neurologists.

We are very proud to support the establishment of a young neurologists and trainees group in New Delhi, conceptualized by Prof. Man Mohan Mehndiratta. We owe Prof. Mehndiratta many thanks for his dedication to young neurologists' issues.

In 2011, Dr. Tissa Wijeratne, originating from Sri Lanka and working in Australia, has joined as second Asian delegate. His advocacy efforts for young neurologists has recently resulted in the initiation of the Asia Pacific Association of Young Neurologists and Trainees (www.apaynet.org). These efforts merged with efforts from Dr. Tanprawate and Prof. Mehndiratta, and we are confident that this will be a strong representation advocating young neurologists for the Asia and the Pacific region.


**The Young Neurologist Workshop in Marrakesh, chaired by Dr. Stephen M. Sergay and Dr. Wolfgang Grisold, featured lively discussion.**

### Australia/New Zealand

The IWGYNT's delegates from the Australian and New Zealand Association of Neurologists (ANZAN), Dr. Kate Ahmad and Dr. Jason Burton, already have a working network of young neurologists via ANZAN. They are currently trying to foster training exchange with other continents.

### Europe

The delegates of the European Association of Young Neurologists and Trainees (EAYNT, www.eaynt.org), Dr. Cristian Falup-Pecurariu and myself, are enjoying a well-working young neurologists network in Europe. We promoted the IWGYNT at many European meetings and several online and print articles and tried to actively interconnect all groups involved.

### North America

There are currently no representatives from North America, but we are in close cooperation with the American Academy of Neurology's Consortium of Neurology Residents and Fellows (CNRF). Members of the IWGYNT are for the second time invited to contribute to the CNRF's meetings at the AAN congress.

### Central America

Dr. Cumara O'Carroll, a committed young neurologist at the Mayo Clinic in Scottsdale, Ariz., USA, is a liaison to the IWGYNT. She is interested in supporting young neurologists in Central America, and together with Dr. Marco T. Medina, she recently initiated an exchange program with Honduras.

### South America

Unfortunately, the IWGYNT has currently cooperations with only individual South American young neurologists.

### WCN 2011

At the 2011 World Congress of Neurology in Marrakesh, Morocco, Prof. Wolfgang Grisold and Prof. Mostafa El Alaoui Faris generously offered a free workshop and a free booth at the congress. The IWGYNT, together with the great support of the EAYNT, organized a free workshop and a booth. Both initiatives were successful and well visited. ■

DR. STRUHAL *is chair of the International Working Group of Young Neurologists and Trainees and a past president of the European Association of Young Neurologists and Trainees. He works in the Department of Neurology and Psychiatry at the General Hospital of the City of Linz (Austria).*

## Calendar of International Events

### 2012

**7th World Congress for NeuroRehabilitation**
May 16-19, 2012
Melbourne, Australia
www.dcconferences.com.au/wcnr2012/Home

**SSIF Annual Meeting in Multiple Sclerosis**
May 18-19, 2012
Valencia, Spain
www.seronosymposia.org

**12th International Conference on Myasthenia Gravis and Related Disorders**
May 21-23, 2012
New York, USA
www.nyas.org/MG12

**Third International Conference "Advances in Clinical Neuroimmunology" ACN 2012**
May 31-June 1, 2012
Vienna, Austria
www.acn2012.eu

**13th Asian Oceanian Congress of Neurology**
June 4-8, 2012
Melbourne, Australia
www.aocn2012.com

**47th Annual Congress Canadian Neurological Sciences Federation**
June 6-8, 2012
Ottawa, Ontario
www.cnsfederation.org/congress.html

**22nd Meeting of the European Neurological Society**
June 9-12, 2012
Prague, Czech Republic
www.congrex.ch/ens2012

**1st African Epilepsy Congress**
June 21-23, 2012
Nairobi, Kenya
www.epilepsynairobi2012.org

**16th Congress of the European Federation of Neurological Societies**
Sept. 8-11, 2012
Stockholm, Sweden
www.efns.org/efns2012

**10th European Congress on Epileptology (ECE)**
Sept. 30 – Oct. 4, 2012
London, United Kingdom
www.epilepsylondon2012.org

**8th World Stroke Congress (WSC 2012)**
Oct. 10-13, 2012
Brasilia, Brazil
www2.kenes.com/stroke/Pages/Home.aspx

### 2013

**XXI World Congress of Neurology**
Sept. 21-26, 2013
Vienna, Austria
www2.kenes.com/wcn/Pages/Home.aspx

## REGIONAL FOCUS: LATIN AMERICA

# Addressing the Need for Reliable Data in Emerging Countries

BY LUCIANO SPOSATO, MD, MBA

*Dr. Sposato is director of the stroke center at the Institute of Neurosciences, Favaloro Foundation University Hospital, and chairman of the department of neurology at INECO (Institute of Cognitive Neurology), both in Buenos Aires.*

BY OSVALDO FUSTINONI, MD

*Dr. Fustinoni is professor of neurology at the Buenos Aires University Medical School and chief of cerebrovascular diseases at the Instituto de Neurociencias Buenos Aires, Argentina.*

The World Health Organization has stated that it is crucial that countries all over the world improve their data collection systems to assess health indicators and measure the impact of public health policies and resource utilization at the population level. This is particularly important for noncommunicable diseases (NCDs) such as cerebrovascular disease in Latin American countries where relevant epidemiological data are scarcely available.

During a United Nations meeting Sept. 19-20, 2011, participants from 113 member states, including 34 heads of state and 2 representatives from the American Heart Association and the World Stroke Organization, analyzed the problem of NCDs, particularly in emerging countries. The main goal was to generate strategies for improvement through coordinated research initiatives and a global monitoring framework, mainly in low- and middle-income countries, where 80% of deaths from stroke and coronary disease occur each year. There was general agreement as to the World Health Organization's (WHO's) coordinating role.

As part of the initiative on improving data collection systems and improving the measurement of public health policies, the WHO has identified three major challenges regarding NCDs:

► The capacity of countries to respond (for example, by improving inadequately funded or nonoperational health infrastructure in many countries, expanding health system capacity and giving a higher priority to NCDs, and developing national NCD programs and policies on stroke).

► Advancing toward multisector action (for example, by systematically engaging the health sector with others across government).

► Monitoring trends and measuring results (for example, through high-quality and adequately supported NCD surveillance of risk factors, outcomes, and health-system responses, with a common set of indicators).

In regard to the third challenge, consistent information of the actual and precise picture of NCDs in most Latin American countries is desperately needed.

Latin American health systems could certainly benefit by improving the volume and quality of research on NCDs. Population-based studies from Latin America are necessary to provide local reliable data and should be specifically designed to represent most populations with low-middle and upper-middle income economies. The inadequate extrapolation of facts from European or North American sources, that surely do not represent the Latin American reality, should be avoided. It is pointless to attempt secondary stroke prevention policies solely on the basis of those sources, without knowing the cause of the initial strokes in the first place. The development of entirely Latin American studies would be the much needed stepping-stone to generate proper public health policies in the region. ■

## MEETING ROUND-UP

# Movement Disorders Course in Tanzania a Success

BY KAREN P. FREI, MD

The World Federation of Neurology Association for Parkinsonism and Related Disorders collaborated with the Medical Association of Tanzania to hold a Parkinson's and Movement Disorders conference at the Protea Hotel Courtyard, Dar es Salaam, on Feb. 11.

The meeting was well attended with approximately 30 physicians from all over the country. The meeting happened to occur following the end of a physician's strike in Tanzania. Dr. Namala Mkopi, the current president of the Tanzanian Medical Society, helped to organize this meeting along with Dr. Tanya Simuni and Dr. Daniel Truong from the United States.

Dr. Simuni of Northwestern University, Chicago, spoke on the differential diagnosis of Parkinson's disease and on the nonmotor symptoms of Parkinson's. I gave a talk about Parkinson's disease and the treatment of Parkinson's disease. In between talks, Dr. Ryan Uitti of the Mayo Clinic, Jacksonville, Fla., USA, demonstrated the proper neurological exam. He also presented information on parkinsonism, dementia, and tremors. Dr. Hubert Fernandez of the Cleveland Clinic in Cleveland, Ohio, USA, presented on the topics of multiple system atrophy, progressive supranuclear palsy, and chorea. Dr. Truong of the Parkinson's and Movement Disorders Institute, Orange County, Calif., USA, spoke on dystonia and other movement disorders, including restless legs syndrome and myoclonus. Some presentations also focused on nonmedication-based treatments such as cueing therapy – walking in time to a metronome beat to improve gait in Parkinson's disease.

Infectious diseases such as HIV/AIDS comprise the majority of health issues in Tanzania, but with advancement in available treatments for infectious disease, and as the population ages, there will be greater numbers of people with chronic conditions such as Parkinson's disease. But resources in Tanzania are limited. The entire country has only three neurologists and one MRI scanner. Many patients continue to use traditional healers or home remedies to help with their symptoms.

COURTESY DR. DANIEL TRUONG

**Faculty and some of the participants of the workshop in Dar es Salaam, Tanzania, on Feb. 11, 2012. In the front row are Dr. Ryan Utti (Mayo Clinic, Jacksonville, Fla., USA), Dr. Karen P. Frei (Parkinson's and Movement Disorder Institute, Orange County, Calif., USA), Dr. Tanya Simuni (Northwestern University, Chicago, USA), Dr. Namala Mkopi from the Tanzania Medical Association, Dr. Huber Fernandez (Cleveland Clinic, Ohio, USA) and Dr. Daniel Truong (Parkinson's and Movement Disorder Institute, Orange County, Calif., USA).**

Currently, the prevalence of Parkinson's disease in sub-Saharan Africa is controversial. Data on this subject are limited, but the few studies that have been conducted reported prevalences lower than in other parts of the world.

A recent study estimated the prevalence of Parkinson's disease in Tanzania to be 20 per 100,000 population, which is still lower than the prevalence reported in the United Kingdom. Patients with Parkinson's disease in Tanzania are usually not diagnosed or treated for the disease, which has been regarded to be a part of the normal aging process by many in the country.

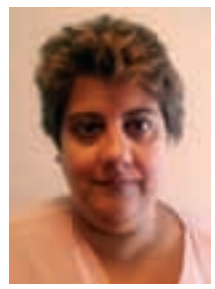
In Tanzania, standard medications used to treat Parkinson's disease are difficult to obtain and expensive. Most patients are unable to afford medication to treat their diseases and they will ration the medications provided by the government. For example, in part of one sociology study in rural Tanzania, 28 patients with Parkinson's disease were identified, the majority of which were not previously diagnosed. Only two were taking medication to treat the symptoms of the disease. ■

DR. FREI *is director of clinical research at the Parkinson's and Movement Disorders Institute, Orange County, Calif., USA.*

# Chagas-Mazza Disease and Stroke: A Call for Attention

## *Emigration of infected patients to developed countries has changed the epidemiology of the disease.*

After malaria and schistosomiasis, Chagas disease is the third most common parasitic infection worldwide, affecting mostly South American populations who have low incomes and restricted access to medical care. It is caused by the flagellate protozoan *Trypanosoma cruzi*. The Brazilian physician Carlos Chagas described the disorder in 1909. In Argentina, it is known as Chagas-Mazza disease, in honor of Salvador Mazza, the Argentine physician who in 1926 investigated and described its epidemiologic cycle and over the years became one of its leading researchers worldwide.



BY MARÍA CRISTINA ZURRÚ, MD

*Dr. Zurrú is a neurologist in the cerebrovascular disease section at the Hospital Italiano de Buenos Aires, Argentina.*

About 14 million people have emigrated to Europe, North America, Japan, and Australia in the past 20 years, many of them asymptomatic infected patients coming from endemic regions. This resettlement, together with that of thousands of others who moved from rural to urban areas in South America, has changed the epidemiology of the disorder, which has consequently become an emerging epidemiologic problem in developed countries. It is believed that Charles Darwin himself may have caught the disease during his voyage to South America in the early 19th century.

The major complications – disabling cardiomyopathy and stroke – occur in the chronic phase. Cerebral infarctions have been described in autopsy series, case-control studies, clinical reports, and cohort studies. Chagasic cardiomyopathy is independently associated with ischemic stroke. Chronic heart disease causes heart failure, several types of arrhythmias, sudden cardiac death, and systemic thromboembolism. The main risk factors associated with ischemic stroke include cardiac apical aneurysm, atrial fibrillation, mural thrombus, and left ventricular dysfunction. Stroke occurs more often in women and younger patients. In contrast, hypertension, diabetes mellitus, dyslipidemia, and smoking are less common in stroke patients with chagasic cardiomyopathy. Other causes of stroke encountered in these patients, such as carotid atherothrombosis and small vessel occlusion, are probably associated with the presence of coexistent atherosclerotic vascular risk and not with chronic arterial inflammation due to parasitic infection.

Educational campaigns are needed to reduce the high infection risk in South America. Currently, around 100 million people live in the endemic regions where *Triatoma infestans* (the household insect responsible for *T. cruzi* transmission) is detected. Approximately 25% have the chronic form of the condition and are at risk of heart failure and subsequent ischemic stroke.

**PATIENTS WITH ISCHEMIC CARDIOEMBOLIC OR CRYPTOGENIC STROKE SHOULD BE IMMUNOLOGICALLY SCREENED FOR *T. CRUZI* INFECTION.**

Early diagnosis and secondary prevention measures should be encouraged in chagasic stroke. Around 20%-25% of infected stroke patients are classified as cryptogenic. Consequently, patients with ischemic cardioembolic or cryptogenic stroke should be immunologically screened for *T. cruzi* infection, especially if they come from endemic regions.

Clinical trials are needed to assess the efficacy of anticoagulant therapy for primary and secondary stroke prevention in this condition. Although some studies have reported an association between chronic *T. cruzi* infection and cognitive impairment with or without ischemic stroke, the relation between ischemic stroke and dementia has not been properly investigated. The World Health Organization control measures initiated against *T. infestans* have had a dramatic effect in lowering the prevalence of the disorder. However, the long latency period before the chronic clinical stage arises will maintain this illness as an important public health problem for decades. Therefore, prior to the indication of any therapy or prevention strategy, the inclusion of Chagas-Mazza disease in the differential diagnosis of stroke is essential. ■

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# New Projects Are Underway in Countries

**Epilepsy** • *from page 1*

Dr. Carlos Acevedo, secretary general of the International Bureau for Epilepsy, to propose the strategy and action plan. They worked with a team of more than 30 experts from Latin America to draft the document, which received final approval at a PAHO meeting in Washington, D.C., USA, on Sept. 29, 2011. PAHO member states agreed to:

► Make epilepsy a national health policy priority by implementing programs that are adapted to conditions in each country.

► Strengthen legal frameworks to protect the human rights of people with epilepsy and effectively enforce relevant laws.

► Strengthen primary care systems and integrated services networks to promote universal and equitable access to medical care for people with epilepsy.

► Ensure the availability of the four antiepileptic drugs that are considered essential for treatment: phenobarbital, phenytoin, carbamazepine, and valproic acid.

► Improve neurological services to detect and manage cases at the primary care level.

► Support effective participation by the community, patient associations, and family members in activities designed to improve the care of people with epilepsy.

► Promote educational initiatives within and between countries to combat stigma and discrimination against people with epilepsy.

► Provide the means to improve the production, assessment, and use of information in the field of epilepsy.

► Strengthen partnerships between the health sector and other sectors and promote collaboration between nongovernmental organizations, academic institutions, and key social actors.

The document is meant to outline a framework for "each country to develop its own agenda specific to its needs," said Dr. Medina, dean of the School of Medical Sciences at the National Autonomous University of Honduras, Tegucigalpa, and third vice president of the ILAE. He noted that the task force will meet again in November 2012 at the Latin American Congress of Epilepsy in Quito, Ecuador, to evaluate the strategy and action plan.

**The document is meant to outline a framework for 'each country to develop its own agenda specific to its needs.'**

**DR. MEDINA**

The Honduras Treatment Gap Project is one example of a national program that Dr. Medina hopes can be applied in other countries to improve community involvement in the care of people with epilepsy and to increase the number of people who receive treatment or prevention services.

**THE HONDURAS TREATMENT GAP PROJECT IS AN EXAMPLE OF A NATIONAL PROGRAM THAT COULD BE APPLIED IN OTHER COUNTRIES.**

The first phase of the demonstration project sought to determine the treatment gap and prevalence of epilepsy in Honduras. In a study of the impact of community interventions on the incidence of epilepsy and the prevalence of active epilepsy in rural Salamá County, incidence declined from 93/100,000 individuals in 1997 to 36/100,000 in 2005 and prevalence declined from 15/1,000 in 1997 to 12/1,000 in 2005, but these were not significant differences. However, the rate of symptomatic epilepsy caused by neurocysticercosis declined significantly from 37% in 1997 to 14% in 2005. Community interventions included an education and media campaign, animal husbandry training for pig farmers, construction of water projects and proper sewage disposal, construction of a maternal and child health clinic, deworming of Salamá County school students, and ongoing taeniasis surveillance (Epilepsia 2011;52:1177-85).

In 1997, the treatment gap for epilepsy in Salamá County was 58%, based on the prevalence of active epilepsy. More recently, a cross-sectional study involving house-to-house screening of 2,000 randomly selected households in the nearby city of Juticalpa found a prevalence of active epilepsy of 6.5/1,000 individuals and a treatment gap of 48% for active epilepsy, according to Dr. Medina and his associates.

Several other efforts are already underway in other Latin American countries that address the PAHO strategy and action plan, Dr. Medina said. In northern Peru, the Bill and Melinda Gates Foundation has provided funding to develop programs to reduce the incidence of preventable epilepsy. In Colombia, new legislation is being introduced that is designed to protect people with epilepsy. Brazil has a demonstrative program supported by the WHO that aims to improve education and reduce the treatment gap for people with epilepsy. Programs in Chile have been successful in improving access to antiepileptic drugs for people with epilepsy. ■

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# Program Highlights Dancing as Therapy for Parkinson's

BY MARK HALLETT, MD
*Editor in Chief,* WORLD NEUROLOGY

Dancing is receiving new attention for its therapeutic value in Parkinson's disease in a network of new dance classes that have spread internationally. One of the most well-known and successful modern dance companies in the United States, the Mark Morris Dance Group (MMDG) is promoting a program called Dance for PD that it developed with the Brooklyn (N.Y., USA) Parkinson Group.

The Dance for PD project at MMDG began in 2001 when Olie Westheimer, the director of the Brooklyn Parkinson Group, conceived the idea based on her experiences in both studying dance and seeing patients. Olie is the wife of neurologist and Parkinson's disease specialist, Dr. Ivan Bodis-Wollner. She approached MMDG, and the program was initiated with support of the dance group itself and some foundation grants.

COURTESY AMBER STAR MERKENS

**Misty Owens leads members of the Brooklyn Parkinson Group at the Mark Morris Dance Center.**

Dance combines physical exercise, mental function, rhythmic stimulation, and a good time. Because it is usually done in a group setting, it also encourages social interaction and friendships. It is likely that patients would more likely continue to participate in it than in a simple exercise such as treadmill running (unless perhaps they can simultaneously listen to music or watch television). The caregiver also benefits from dance.

There is already published evidence that tango provides benefits to patients. In one study, there was a head-to-head comparison between tango and American ballroom dancing, and tango seemed slightly better, although both were good.

A developing body of data shows that dance has value for gait, balance, fatigue, quality of life, and enjoyment. It also is well established that physical activity is good for a person's health and longevity, and that both physical and mental activity are good for maintaining cognitive function. Physical and mental activity are valuable for the average healthy person, and appear to be doubly valuable in patients with Parkinson's disease. Physical activity works in many ways, including the production of an important neurotrophic factor, called brain-derived neurotrophic factor.

The dance classes at MMDG are firmly based on the fundamental principles of instruction that inform all forms of dance; these principles apply not only to the physical act of dancing, but they also place considerable emphasis on cognitive aspects such as rhythm, sequencing, creativity, and aesthetics. The teaching of choreography in classes brings all these aspects of dance into focus.

The Dance for PD program has spread internationally, and now has more than 1,500 students in 60 locations in the USA, Europe, and India who participate in classes based on the original Brooklyn model.

COURTESY DR. MARK HALLETT

**David Leventhal (left), the program manager and an active teacher for Dance for PD, meets with the director of the Brooklyn Parkinson Group, Olie Westheimer, and her husband, Dr. Ivan Bodis-Wollner, a neurologist and Parkinson's disease specialist.**

The program also trains teachers in the methods and approaches that seem most successful. The Dance for PD network is rapidly expanding, and the program will shortly have a series of videos available to introduce the fundamental method to patients who can't attend a class or for patients who want to practice between classes.

Parkinson's disease, like most diseases, should not be treated with medications alone. Lifestyle and activity are also important. Dopaminergic medications and maybe also deep brain stimulation are helpful, but so too is dance. Why not get better and have fun at the same time? ■

*More information about Dance for PD is available at danceforparkinsons.org.*

## WFN ASIA INITIATIVE

# 'Let's Share a Dream'

RYUJI KAJI, MD

In his 2010 inauguration speech, World Federation of Neurology President Vladimir Hachinski conveyed a clear message: "Asia has more than 60% of the global population, yet in some areas, the education of neurology to young neurologists does not keep up with the patients' needs of neurological care. For this reason, it is essential for WFN to help vitalize the educational activity in this region among others."

Since I was appointed as the head of the Asia Initiative, I have been trying to promote the educational activities in neurology with the aid of many friends inside and outside Asia. It is for this reason that I invite you to attend the Asian-Oceanian Congress of Neurology (AOCN) 2012 meeting in Melbourne, Australia, June 4-8.

Prof. Matthew Kiernan of Australia, the AOCN program chair, and Prof. Ching Piao Tsai of Taiwan, the President of the Asian-Oceanian Association of Neurology (AOAN), are trying their best to plan an attractive program with speakers from all over the world for AOCN and other educational courses, and to find as many sponsors as possible to improve the financial status of the meeting. Prof. Tsai and his colleagues have decided to hold the AOCN every 2 years instead of every 4 years, and if the congress is a success, future meetings could attract more and more people over the years, and might be held every year. A successful meeting will mean that Asian and Oceanian societies are now getting closer to becoming a unified neurology organization.

I have talked with Prof. Tsai and his colleagues, and it is clear that we share a dream of having an annual meeting in the future that is comparable with the European Federation of Neurological Societies congress in Europe, or the American Academy of Neurology meeting in North America.

We met last November at the World Congress of Neurology in Marrakesh, Morocco, and had an Asia Initiative meeting. A total of 17 people from inside and outside the region attended the meeting and had many productive discussions. We reached three major points to pursue in our future activities:

► First, it is important for associations to hold meetings in collaboration with one another. It is strategically important to use existing frameworks, including AOCN. We could ask the ASEAN (Association of Southeast Asian Nations) Neurological Association, which is headed by Prof C.T. Tan of Indonesia, and the East Asian Neurology Forum (an informal get-together of those from Korea, Taiwan, China, Hong Kong, and Japan) to synchronize meetings, so that a large attendance can be expected. Joint meetings between any of these two organizations are now being planned for the 2014 AOCN meeting in Hong Kong.

► Second, it is essential to work with other international organizations, such as the Movement Disorder Society or the International Federation of Clinical Neurophysiology. Both of these organizations have agreed to have a satellite basic movement disorder course or a basic EMG hands-on course at the AOCN 2012 meeting.

► Third, we will ask groups of young neurologists to join these activities through the Internet. This promising idea was proposed by Dr. Tissa Wijeratne of Australia, who also represents Sri Lankan neurologists. He is now forming the Asia Pacific Association of Young Neurologists and Trainees.

We need your help for this dream, which also embodies that of WFN itself. Please come and join AOCN 2012 for a wide variety of educational opportunities at a reasonable cost for travel, accommodation, and registration. ■

*DR. KAJI is a WFN Trustee.*

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# Surgical Removal Boosts Brain Thrombus Recovery

BY MITCHEL L. ZOLER
*Elsevier Global Medical News*

NEW ORLEANS – An investigative, minimally invasive surgery for reducing intracranial clot volume following an intracerebral hemorrhage showed promise in results from a randomized trial.

In the controlled study, 54 patients who underwent clot removal by minimally invasive surgery (MIS) had a 10% increased rate of achieving a modified Rankin Scale (mRS) score of 1-3 at 180 days, compared with 39 patients managed by conventional, medical therapy, Dr. Daniel F. Hanley said at the International Stroke Conference.

MITCHEL L. ZOLER/IMNG MEDICAL MEDIA

**Minimally invasive clot removal improved outcomes, Dr. Daniel F. Hanley said.**

"These data may establish a surgical goal for MIS of reducing clot burden to 15 mL or less by 3-4 days" after the intracerebral hemorrhage (ICH), said Dr. Hanley, a professor of neurology and neurosurgery at Johns Hopkins University in Baltimore, Md., USA. The study enrolled patients within a day of their ICH with a clot volume of at least 20 mL; the average volume for the 93 patients was 40 mL.

The next step will be a pivotal, controlled study planned to enroll 500 patients at 35-50 centers, with an expected study duration of 5 years. Dr. Hanley and his associates are seeking funding from the U.S. National Institutes of Health.

The study used a combination of intracerebrally infused recombinant tissue plasminogen activator (rTPA) and placement of a cannula into a patient's skull to remove thrombolysed clot, a method that "has been around" for several years, but never before underwent assessment as a standardized procedure and in a prospective, controlled study, Dr. Hanley said in an interview.

The study enrolled patients at 35 international sites who were 18-75 years old and had a spontaneous, supratentorial ICH with a stable clot. They also had received rTPA within 54 hours of their first diagnostic CT examination. The mean age of the enrolled patients was 61 years, two-thirds were men, and the patients randomized to MIS received their initial rTPA treatment an average of 48 hours after the ICH began. During an initial phase of the study patients received 0.3 mg of rTPA, but during the later phase the dose increased to 1.0 mg, the amount that most of the MIS patients received.

Safety data showed that patients treated with MIS had a 7-day mortality rate of 2 and a 30-day mortality of 15%, compared with a rate of 8% at 30 days in the medically treated control patients. Symptomatic bleeds occurred in two of the MIS patients and one of the controls, and a brain infection occurred in none of the MIS patients and in one control patient. During follow-up out to 180 days, mortality rates were virtually identical, about 20%, in both arms of the study, and dropouts also reached similar levels in both arms, about 45%.

During their first 4 days in the study, MIS patients had an average 65% reduction in their intracerebral clot volume, compared with no change in the control patients. The two-thirds reduction with MIS corresponded to an average 28 mL drop in volume.

The study's primary outcome was mRS at 180 days, with data available for 50 MIS patients and 33 controls. No patients in either group had an mRS of 0. An mRS of 1 occurred in two MIS patients and none of the controls. An mRS of 1-3 occurred in about 35% of the MIS patients and about 25% of the controls.

The prespecified goal of MIS was removal of at least 15 mL of clot, and surgeons achieved this in about a third of the MIS patients. When patients attained that level of clot reduction, they had a statistically significant, 3.7-fold increased rate of having an mRS of 1-3 at 180 days, compared with patients who did not reach this goal.

Among the subgroup with a clot burden of at least 50 mL, MIS led to a 17% increased rate of patients achieving an mRS of 1-3, compared with the controls, Dr. Hanley said. Among patients treated medically, those with a clot burden on entry of about 20 mL often had an mRS of 1-3 at 180 days, but among those who began with a clot of at least 30 mL, only three patients reached an mRS of 1-3. ■

**COMMENTARY**

The minimally invasive surgery tested in this study is probably the most promising approach developed for treating the devastating disease of intracerebral hemorrhage.

The results showed a 10% increase in the rate of patients recovering to a modified Rankin Scale score of 1-3; it is a pretty significant result. It results in less disability for patients and less burden to their families.

The most important predictor of outcome was the size of the clot; if you can do anything meaningful to reduce the size, it should benefit patients. But aggressiveness in removing clot must be balanced against minimizing manipulation of brain tissue. The goal is to remove as much clot as possible without doing damage. The results did not include information on brain edema following surgery, but it looks like despite the trauma of intervention patients on balance had better outcomes.

This was a phase II study, so the results now need to be replicated in additional patients. At this point, it remains ethical to randomize patients to receive either this treatment or conventional therapy. This is a very important treatment to further examine.

*DR. STEVEN R. LEVINE is professor of neurology and emergency medicine at the State University of New York Downstate Medical Center, Brooklyn, N.Y., USA. He said that he had no disclosures. Dr. Levine made these comments in an interview.*

# Need for CT Perfusion Imaging in Acute Stroke Questioned

BY MITCHEL L. ZOLER
*Elsevier Global Medical News*

NEW ORLEANS – The extra time needed for CT perfusion imaging in patients with an acute ischemic stroke may not be warranted, based on a retrospective analysis of 418 patients treated at nine U.S. tertiary stroke centers.

The analysis showed that the outcomes in patients assessed using CT perfusion (CTP) were very similar to those in patients worked up with noncontrast CT (NCCT), and that CTP added an average of 48 minutes to the time elapsed between the start of imaging and the completion of the reperfusion procedure, Dr. Rishi Gupta said at the International Stroke Conference.

"Additional imaging did not translate into better clinical outcomes or reduced hemorrhage rates, raising the question of whether NCCT is good enough," said Dr. Gupta, a neurologist at Emory University and director of the acute stroke network at Grady Health System, both in Atlanta, Ga., USA.

Because the analysis was retrospective, the next step is a prospective, randomized study to compare the impact of NCCT and CTP, Dr. Gupta noted. Despite this limitation, he said he and his associates at Grady Health are convinced by the findings and have already scaled back their use of CTP to rely more on NCCT.

"We cut back quite a lot on our CTP based on these findings," although a majority of centers that perform endovascular perfusion on acute stroke patients "tolerate the delay and get CTP," he said in an interview. "We need to do a randomized study" to settle the question, he added.

The data set compiled from the nine participating U.S. centers included 418 eligible patients who underwent imaging prior to endovascular reperfusion therapy between September 2009 and December 2011. Of these, 227 (54%) had CTP and 191 (46%) had NCCT.

The study included consecutive patients with an occlusion of the middle cerebral or internal carotid artery treated within 8 hours of symptom onset. The analysis excluded patients with a posterior circulation stroke, those who underwent MRI, and those with a thrombus in their anterior cerebral or distal middle cerebral artery. The patients' average age was 67 years, and their average National Institutes of Health Stroke Scale score was 18.

The analysis showed successful reperfusion in 65% of the NCCT patients and in 71% of those imaged with CTP. A good clinical outcome – a modified Rankin Scale score of 0-2 at 90 days after hospitalization – was achieved in 37% of the NCCT and 38% of the CTP patients. Mortality was 23% in the NCCT and 21% in the CTP patients. The rates of symptomatic and asymptomatic hemorrhage were also similar in the two subgroups. None of these between-group differences were statistically significant. In a multivariate analysis, the use of CTP was not a significant determinant of a good clinical outcome.

Average time from the start of CT imaging to reperfusion was 175 minutes in the NCCT patients and 223 minutes in the CTP group.

Dr. Gupta presented two additional analyses designed to compare outcomes using the two imaging methods in closely matched subgroups. In one analysis, he focused exclusively on the 291 patients in the database who had occlusions at the M1 site of the middle cerebral artery. In these patients, NCCT saved an average of 40 minutes, compared with CTP, and outcomes were not significantly better with CTP. In the second analysis, he categorized patients by their Alberta Stroke Program Early CT Score (ASPECTS). In the subgroup of 198 patients with an ASPECTS of more than 7 on a scale of 10, with 10 being normal, CTP did not lead to significant improvement in outcomes and took an average of 45 minutes longer to reperfusion, compared with NCCT.

Dr. Gupta has been a consultant to Concentric Medical, CoAxia, Rapid Medical, and Codman. ■

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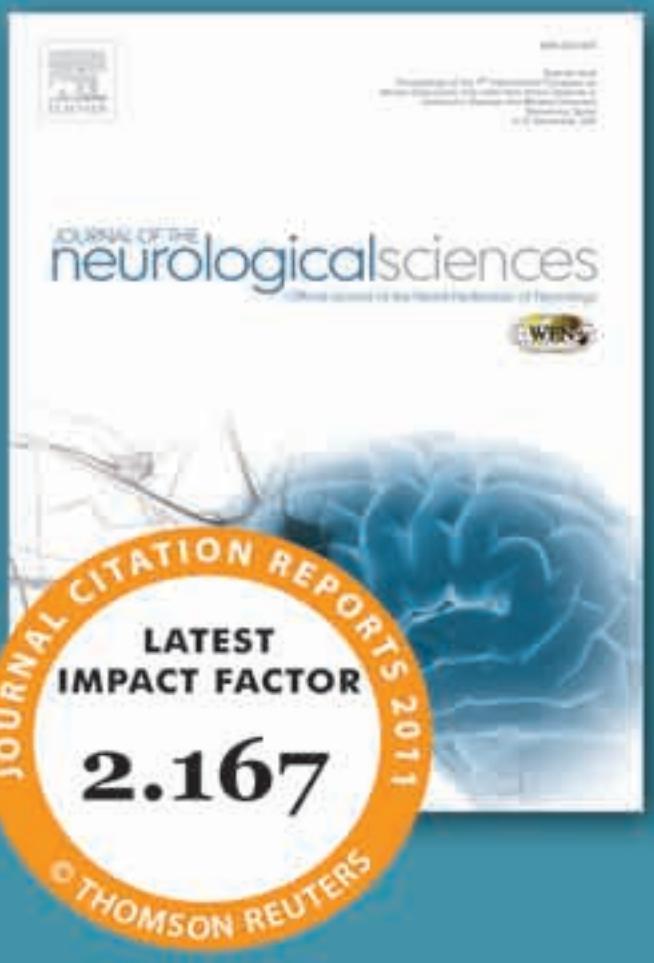


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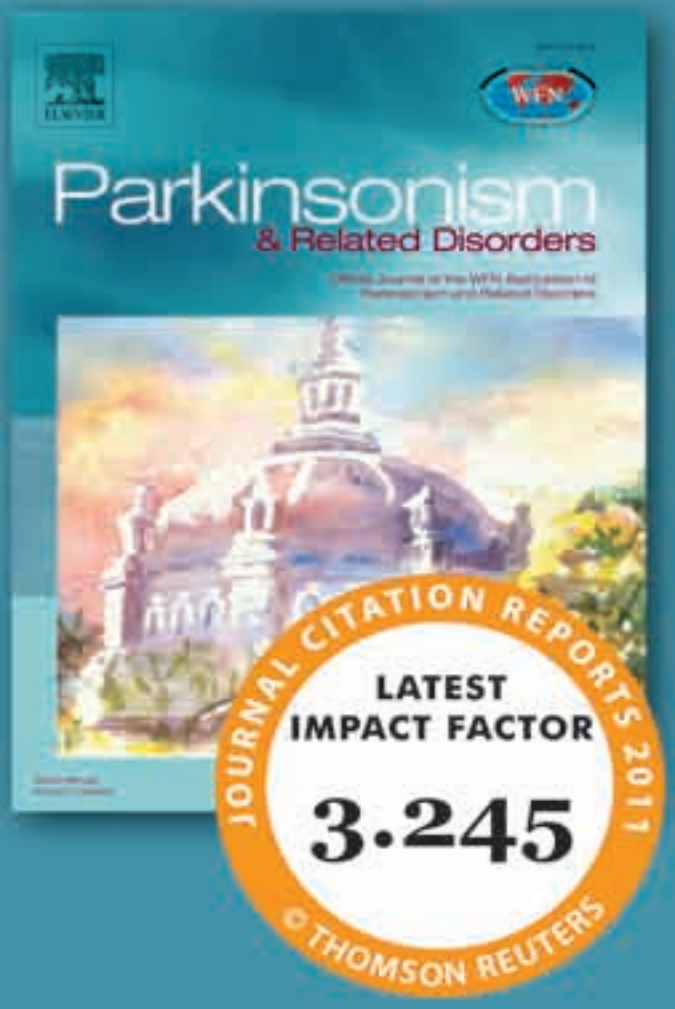


ELSEVIER

OBITUARY

# Richard Koch Olney (1947-2012)

BY MICHAEL J. AMINOFF, MD, DSC

Richard Koch Olney died peacefully on Jan. 27 from amyotrophic lateral sclerosis, a disorder on which he had focused his energy as a physician, educator, and clinical investigator for many years before he himself was diagnosed with it.

He was born in Munich, Germany, in 1947, where his father was an engineer in the U.S. Army. After a year in Germany, several years in West Virginia and other parts of the United States, and a year in Japan, the family finally settled in Oklahoma. He did his undergraduate studies at the University of Pennsylvania, Philadelphia, USA, and the University of Oklahoma, Norman, USA, following which he went to Baylor University, Houston, Tex., USA, where he received his MD degree in 1973. He then began residency training in psychiatry at the University of California, Los Angeles, USA, but soon transferred to the neurology program at the Oregon Health Sciences University (OHSU) in Portland, USA, becoming a board-certified neurologist in 1980. After a brief stint in practice, he joined the faculty of OHSU before moving to the University of California at San Francisco (UCSF), where he became an associate professor in 1989 and a full professor in 1995.

He was appointed Associate Editor of Muscle & Nerve in 1998, and to the editorial board of several other journals shortly thereafter. He held a number of offices in the various professional organizations to which he belonged. He was the author of numerous original papers, review articles, and book chapters relating to his research interests, which initially focused on the use of electrophysiological techniques to investigate the operation of the neuromuscular system in health and disease and, more recently, on amyotrophic lateral sclerosis (ALS). Indeed, he personally created and directed the Comprehensive ALS Center at UCSF, and it is a cause for sadness that he himself eventually became a patient there, being cared for with devotion by the very staff whom he had trained. His unit became one of the most respected units in the country. He had not merely knowledge but the wisdom to know how best to use that knowledge. That is a rare skill among clinicians and is what distinguishes the outstanding physician from the mediocre.

He worked long hours, many being devoted to patient care. He always seemed to be calling patients with advice, support, and encouragement, and his compassion and kindness helped ease their distress and fears. He also had the rare ability to inspire others, his trainees, by his own example. He was a great clinical teacher who could let others know what they did not know without upsetting or hurting them. He befriended many of his students and never sought their thanks for the quiet help that he gave them. He had a first-class mind and the temperament of a gentleman.

He also deliberately and courageously publicized his illness with the hope of increasing awareness of the disease, becoming a national spokesperson on ALS. His efforts were rewarded by the Lifetime Achievement Award of the American Association of Neuromuscular & Electrodiagnostic Medicine, and by an award for public education from the American Academy of Neurology Foundation. The sad irony of his personal plight captured the attention of the media and, in the numerous articles that appeared about him in the national press and on radio and television programs, he discussed the nature of the disease, the importance of basic and clinical studies, and the need for controlled clinical trials of potential therapies. He thereby gave ALS a human face and dimension, coming to personify the disease to the general public and national agencies, both in the United States and overseas. This may yet prove to have been his greatest achievement, for it will undoubtedly help both individuals trying to cope with the disease and those concerned with advancing its treatment. ■

COURTESY ALS ASSOCIATION

**Through numerous articles and radio and TV appearances, Dr. Richard Koch Olney's personal battle with ALS gave the disorder a human face and dimension.**

DR. AMINOFF *is director of the Parkinson's Disease and Movement Disorders Clinic at the UCSF Medical Center.*

# Clinical Presentation Varies

**Mutation** • *from page 1*

9 [doi:10.1016/S1474-4422(12)70043-1]).

The discovery of the mutation and the subsequent characterization among patients who have FTD, ALS, both FTD and ALS, or primary progressive aphasia are just the first steps of many before treatments can be based on the new knowledge, said Dr. Paul Schulz of the department of neurology at the University of Texas, Houston, USA, where his lab examines the mechanisms underlying normal cognition and neurodegenerative disorders.

To illustrate his point, Dr. Schulz cited how the genes for myotonic dystrophy and Huntington's disease were discovered in 1992 and 1994, respectively, but researchers still know little about them. "We don't know what they do, how the mutations cause problems, and how to replace them."

Preliminary findings underpinning the discovery of C9ORF72 were made in 2006 when investigators discovered that either FTD and ALS or a combination of both diseases were linked to a region on chromosome 9p21 in members of some families with the diseases. The big step came in September 2011 when two research groups independently identified the precise nature of the long-sought-after mutation (Neuron 2011;72:245-56; 257-68). It proved to be a GGGGCC hexanucleotide repeat in the noncoding region of the C9ORF72 gene.

**The discovery and characterization of the mutation are the first steps of many before treatments can follow.**

DR. SCHULZ

Originally, no mutation had been found even after repeated sequencing of the investigational region on chromosome 9p21, but eventually, the two research groups examined the pattern of inheritance and noticed that only the good gene appeared to be inherited rather than one gene from each parent.

"After various experiments, it was realized that the abnormal gene was invisible to gene sequencing because the hexanucleotide bound to itself," related Dr. Schulz. "As a result, it was impenetrable by normal PCR [polymerase chain reaction] amplification. Now that this mechanism of mutation is known, I'm sure gene hunters are looking for others that are also 'silent.' "

## Mutation Screening in FTD and ALS

In the Lancet Neurology study of 4,448 ALS patients and 1,425 FTD patients from the United States, Europe, and Australia, researchers found the C9ORF79 mutation in 7% of sporadic ALS in white patients and 4.1% of black patients. It was present in 6% of white patients with sporadic FTD. The results of those with familial FTD or ALS were more surprising, with the expansion present in 38% of all patients with familial ALS and 25% in white patients with familial FTD.

A series of four papers published in Brain by groups from the Netherlands; Manchester, England; London, England; and the Mayo Clinic in Rochester, Minn., and Jacksonville, Fla., USA, reported the results of screening large cohorts of patients with FTD totaling nearly 1,200 cases. Overall, 7%-12% of the cohorts were found to have the mutation (Brain 2012;135:693-708; 723-35; 736-50; 765-83).

Another two papers and the same Mayo Clinic paper reported on the frequency of the mutation in patients with ALS. In 563 ALS patients from northern England, including 63 with a family history of ALS, the C9ORF72 expansion was found in 11%, but it occurred more often among patients with familial disease (43%) than with sporadic disease (7%) (Brain 2012;135:751-64).

Among patients with familial ALS, the mutation occurred in 38% of 141 Italian cases (including 57% in 21 Sardinian cases) and in 22% of 41 German cases (Brain 2012;135:784-93).

Mayo Clinic researchers detected the mutation in 7% of 229 ALS patients and in 24% of 34 patients with familial ALS, parkinsonism, or dementia. Only 4% of sporadic ALS cases had the mutation. Among patients with a clinical phenotype of FTD and ALS, the prevalence of the mutation was 22%, but it approached 50% among those with a positive family history (Brain 2012;135:765-83).

"All of these statistics mean that this hexameric repeat is fairly common amongst those with familial FTD or ALS, or especially FTD with ALS," according to Dr. Schulz. But familial FTD was present in only 40% of those with FTD, and familial ALS was present in only 5% of ALS patients, he noted.

"This means that most sporadic FTD,

*Continued on following page*

BOOK REVIEW

# History of Neurology Text Is a Welcome Addition

***Eminent Neuroscientists: Their Lives and Works***
**By K.B. Bhattacharyya**
**Kolkata, India: Academic Publishers and Association of Neuroscientists of Eastern India; 2011; 443 pp.**

BY FRANÇOIS BOLLER, MD, PHD

*Dr. Boller is a neurologist in Bethesda, Md., USA.*

Most neuroscientists love history. Try to solicit any of the common search engines with the words "history of neurology" and you will find an amazing number of results, many more than for the history of other disciplines. This interest in history is apparent not only in the number of books and articles published on the subject, but also in the number of associations focused on the history of neurology. Those are to be found within each of the major professional groups, starting with the World Federation of Neurology, the American Academy of Neurology, the American Neurological Association, the International Brain Research Organization, and the European Federation of Neurological Societies; and there is of course the International Society for the History of the Neurosciences and its associated journal.

For his book, Dr. Kalyan B. Bhattacharyya has chosen to follow the person-by-person approach, as did his illustrious predecessors Dr. Webb Haymaker[1] and Dr. Haymaker and Dr. Francis Schiller[2] – and also to some extent Stanley Finger, Ph.D.,[3] although the latter embeds the history of the pioneers within an essay dealing with the science world around them. Like those above authors, Dr. Bhattacharyya includes only European and U.S. personalities, with the lion's share devoted to those in the United Kingdom, Germany, and the United States.

French neurologists are also included, but to a lesser extent, since only three "modern age" neurologists (Théophile Alajouanine, Pierre Marie, and the Uzbekistan-born Konstantin Tretiakoff) are discussed. The author rightly acknowledges, albeit only in passing, the contribution of Jean Lhermitte, but he does not mention his son, François Lhermitte. Other noticeably omitted French neurologists include Georges Guillain and Henri Gastaut, even though they all are "household names" among most neurologists.

Dr. Bhattacharyya provides a reference dealing with neurologists from his own country (India), but perhaps a subsequent edition could include some prominent neurologists and neuroscientists from other parts of the world. With the exception of Sir Andrew Huxley, the author includes only persons "who are no longer with us." It is a pleasant surprise to find biographies of persons many of us may have known, such as Norman Geschwind, C. David Marsden, John Newsom-Davis, and Fred Plum.

This person-by-person approach to the history of neurology is complemented by books written in the more narrative format that was followed by Fielding H. Garrison in "Garrison's History of Neurology" (still available in a new edition revised by Dr. Lawrence McHenry),[4] and by the newest addition to the field in the monumental "Handbook of Clinical Neurology," edited by Dr. Finger and his colleagues.[5] These latter sources allow one to follow developments in the field more easily than in the book by Dr. Bhattacharyya, who has chosen to present his characters in alphabetical order (albeit with content divided into "the Beginning" and "the Modern Age").

In terms of content and form, the more than 400 pages in "Eminent Neurologists" are a pleasure to read. Dr. Bhattacharyya's choice of characters is, on the whole, quite judicious. His writing style is light but appropriate, and he narrates personal anecdotes with gusto, bringing those "giants" down to real earth. He accompanies each article with a picture (with a few exceptions), and for this he must be commended because that alone must have represented an enormous amount of work.

There is another nice feature: Dr. Bhattacharyya makes a point of providing the reader with the names of people who have written extensive reviews of the life and work of the neuroscientists he mentions, such as Michael Aminoff's work on Charles-Édouard Brown-Séquard. He tends to be historically accurate (with a few exceptions).

As can be expected (and forgiven), the length and depth of the articles vary a great deal. Less expected and often hard to swallow is, in too many instances, a poorly proofread text with misspellings not only of foreign words, but also of the very name of the persons he writes about. For instance James Papez's name is correct in the title and at the beginning of the article, but further down the page, the famous circuits become "Papaz Circuits" and five lines down "Paper Circuits." Quick, Dr. Bhattacharyya, bring us soon a new edition with these errors corrected, and your book will be an even greater delight to read. ■

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ALS, or FTD-ALS patients are not accounted for. In sporadic FTD, which is more common than familial FTD, then the rate of C9ORF72 mutations appears to be between 2% and 5%," Dr. Schulz said.

### Effect of Other FTD/ALS Mutations

The new C9ORF72 expansion joins two other mutations found in patients with FTD and/or ALS, namely, those affecting the genes for microtubulin-associated protein tau (MAPT) and progranulin (GRN). In a commentary on the studies featured in Brain, Dr. John Hodges of Neuroscience Research Australia and the University of New South Wales in Sydney, Australia, noted that the results of the London-based group (Brain 2012;135:736-50) provide some insight into how likely it is that a patient would have a C9ORF72 mutation and whether this likelihood could be predicted based upon family history and clinical features.

The researchers found that the prevalences of the three mutations were roughly equal in their sample. They also found – based on their Goldman scoring method for quantifying family history – that 88% of patients with a score of 1 (representing an autosomal dominant family history of FTD or ALS) had a mutation in one of those three genes.

However, the Mayo Clinic samples suggest that the C9ORF72 mutation is the most common FTD mutation, present in one-third of people with a family history.

### Links Between FTD and ALS

The C9ORF72 mutation may also provide some insight on the links between FTD and ALS. In all cohorts, the prevalence of C9ORF72 was highest in those with FTD/ALS at 20%-40%, and approached 50% among FTD/ALS cases with a positive family history. Dr. Brad Dickerson, director of the frontotemporal dementia unit and laboratory of neuroimaging at Massachusetts General Hospital in Boston, Mass., USA, said that linking FTD and ALS through this gene was especially important because it would likely lead to research that sheds light on what causes cells in different parts of the brain to be vulnerable in both of these diseases.

**It's still a puzzle why the mutation causes ALS, FTD, and/or primary progressive aphasia in different patients.**

**DR. MESULAM**

"This once again underscores the value that studying one neurodegenerative disease can have for other neurodegenerative disease," he said. "In the case of this gene, advances in understanding its role in FTD will have direct implications for understanding its role in ALS, and vice versa."

Dr. Marsel Mesulam, director of the cognitive neurology and Alzheimer's disease center at Northwestern University in Chicago, USA, said that "exactly how the hopes raised by the C9ORF72 finding will be realized is currently unclear, since we do not yet fully understand the function of C9ORF72." He added that the discovery also generates new puzzles. "Why does the same type of mutation cause ALS in some patients, behavioral FTD in others, and PPA [primary progressive aphasia] in still others?"

### Behavioral Variant FTD Most Common

The behavioral variant of FTD was the most common clinical phenotype associated with the C9ORF72 expansion, and was often accompanied by features of ALS as the disease progressed.

Some studies showed that patients with the C9ORF72 mutation also presented with progressive nonfluent aphasia. Major psychiatric symptoms also were very common, but more details are needed, Dr. Hodges wrote.

### Who Should Undergo Screening?

Given that some patients had the C9ORF72 mutation even without a strong family history, "the most important immediate clinical implication is that we will likely begin screening patients for this mutation once a standard laboratory test for this gene becomes available," Dr. Dickerson said.

In a commentary, Rosa Rademakers, Ph.D., of the Mayo Clinic in Jacksonville, Fla., USA, argued that the use of a clinical screening algorithm may not work because detailed information about family history is often unavailable. At the moment, caution is advised on testing because "our present understanding of the disease penetrance and range of clinical phenotypes associated with this mutation is poor and the smallest repeat size needed for pathogenicity is unknown," Dr. Rademakers wrote.

The sources interviewed for this article did not have any relevant financial disclosures. Dr. Rademakers disclosed that she has a patent pending on the discovery of the hexanucleotide repeat expansion in the C9ORF72 gene. ■

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