

# WORLD NEUROLOGY

THE NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

VOLUME 16, NUMBER 2, JUNE 2001

## PRESIDENT'S COLUMN

It is my hope that this column reaches the WFN membership before the London Congress. I have watched and participated in the extraordinary preparations for this major event, implemented by the Organizing Committee of the Association of British Neurologists. As was said by one of Britain's greatest - "Never have so many owed so much to so few." All of us are deeply indebted to our English colleagues who have gone to such lengths to ensure its success, despite misfortunes, such as the global economic downturn and bovine epizootic encephalitis.

There cannot be a more appropriate time to remind the public that two Nobel prizes



*Earls Court, the venue of the XVII World Congress of Neurology in London.*



*National Institute of Neurology and Neurosurgery, Mexico City. Left to right: Ignacio Ruiz, Head of Postgraduate Teaching; Julio Sotelo, General Director; Teresa Corona, Teaching Director; James Toole, President, World Federation of Neurology; Ricardo Colin, Head of Pre-graduate Teaching.*

have been awarded to neurologists for delineation of mode of transmission and identification of the agent of transmission but we do not have a treatment, other than preventing spread. We must apply our skills to developing an effective prophylaxis and therapy.

Furthermore, neurologists have a responsibility for devoting ourselves not only to human nervous system disorders but those of all animals, because BSE makes us acutely aware of our global interdependence not only with each other but with all flora and fauna.

There is great concern regarding human and other animal rights and, in the past, we have been callous regarding standards for clinical research on lower orders. Neuroscientists must interact with society to agree upon and enforce ethical standards for use of all species. It is no longer tolerable for us to stand by idly and permit

the wanton killing of tigers for medicinal purposes, of rhinoceri and elephants for ivory and for aphrodisiacs, or people whose value to society is judged to be marginal.

Even though we neurologists are few in number, we are highly visible because we are the explorers of the brain, the most important organ in the body. The brain keeps society moving and serves to direct it. We

*(cont. on page 3)*

### ALSO IN THIS ISSUE:

- Editorial
- WFN Annual Reports
- Acute Stroke Units in Austria
- Vascular Dementia
- Mitochondrial Encephalomyopathies
- Book Reviews
- Meetings Calendar

Visit the WFN website at <http://www.wfneurology.org>

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**CONTENTS**

<b>President's Column</b> . . . . .	<b>1</b>
<b>Editorial</b> . . . . .	<b>3</b>
<b>WFN Committee Meetings at the AAN</b> . . . . .	<b>5</b>
<b>WFN Task Force on Neurological Services</b> . . . . .	<b>5</b>
<b>Annual Reports of WFN Research Groups Year 2000</b> . . . . .	<b>5</b>
Research Group on Neuroepidemiology . . . . .	5
Research Group on the History of Neurosciences . . . . .	6
Autonomic Disorders Research Group . . . . .	6
CSF Research Group . . . . .	6
Neurotoxicology Research Group . . . . .	6
<b>Acute Stroke Units in Austria</b> . . . . .	<b>7</b>
<b>Pan-Arab Union of Neurological Sciences</b> . . . . .	<b>7</b>
<b>WFN Junior Travelling Fellowship Reports</b> . . . . .	<b>8</b>
<b>First LACTRIMS Congress</b> . . . . .	<b>8</b>
<b>Vascular Dementia: it is time for a new approach</b> . . . . .	<b>8</b>
<b>Mitochondrial Encephalomyopathies</b> . . . . .	<b>11</b>
<b>Book Reviews</b> . . . . .	<b>13</b>
<b>Meetings Calendar</b> . . . . .	<b>16</b>



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## EDITORIAL

Large numbers of neurologists and other neuroscientists are looking forward to a scientific bonanza at the next World Congress during the British summer in London this month. There have been great scientific advances in neurology since the last World Congress in Buenos Aires in 1997. The mapping of the human genome and the possibilities of gene therapies increase the chances for effective treatment for some of the genetically linked neurological disorders. Let us await with interest the important research in this area which will be revealed at the XVII World Congress of Neurology in London. Around 3,000 persons are already registered with more pouring in everyday; and, if one goes by previous Congress estimates, 20–25% of attendees register 'on the spot'. Therefore, the London Congress is expected to be a great success.

Dr. James F. Toole in his President's Column has reminded all neurologists of their responsibilities towards humans and equal care for animals. He has rightly called neurologists the 'explorers of the brain', the most important organ in the body and he is also right in reminding neuroscientists of the need both to guard human values and protect the rights of animals to exist in their natural environments. He has touched upon some other pertinent questions for neurologists to ponder, concerning questions of neuroethics and the updating of medical ethics etc.

Burglars struck at the World Federation of Neurology office in the heart of London during the night of 18/19 April. The loss of equipment and precious data will be diffi-

*(President's Column – cont. from p. 1)*

cannot afford to have impaired individuals in leadership positions - pilots flying airplanes or leaders of nations making faulty decisions and, yes, impaired doctors making decisions regarding their patients. For these reasons, I am a strong advocate for the World Federation of Neurology assuming global leadership in the field of neuroethics and inviting members of other disciplines to participate with us, through the World Health Organization, in updating the codes of medical ethics, including the right to self determination regarding the end of life and the protection of impaired individuals from the predators who exist in every society. The WFN should embrace its global mandate because it now has an unparalleled communications network and could become the

cult to recover from and this is obviously a matter of great concern. Nevertheless the administrative team of Keith Newton and Susan Bilger, with their ability, zeal and enthusiasm, will again try to rebuild the database as quickly as they can. With the support of national neurological societies, individuals and others they hope to return to normal operations in as short a time as possible.

Annual reports for year 2000 of some of the WFN Research Groups are printed in this issue. They reflect the amount and magnitude of the work that is being carried out by some of the more vibrant groups and the plans that others are formulating.

The report of the Pan-Arab Union of Neurological Sciences is also featured here. It is heartening to learn that this group is fast emerging and accelerating the progress of neurology in this part of the world.

Elsewhere on the globe, the Latin American Committee for Treatment and Research in Multiple Sclerosis (LACTRIMS) also deserve our applause for their 1st Congress and our encouragement for the planned 2nd Congress in 2002. It is a newly formed group but the quality of their performance is self-evident.

Many nations need to emulate the example of Austria, a nation of 8 million people. The report "Acute Stroke Units in Austria" by Prof. Michael Brainin, President of the Austrian Society for Stroke Research, is illuminating and reveals the masterly planning that has been put into the aim of doubling the present twenty-five functional stroke units in that country by 2005. This will be a quite fantastic feat and they deserve our congratulations for their efforts.

intellectual pacesetter because neurologists can relate to philosophy, ethics, and religion in unique ways.

Within the past few months, I attended the American Stroke Association meeting, which has grown from perhaps 50 dedicated individuals, of which I was one, to nearly two thousand attendees. Although this multi-disciplinary group involves primarily neurologists, I am struck with the reality that the World Federation of Neurology has no group dealing with stroke. Our research group, founded by Helmut Lechner and John S. Meyer, has been dissolved. It is my strong belief that neurologists must be the primary care givers for stroke victims but that we have abdicated our responsibility. We must resurrect our presence and restructure ourselves into the premier group dealing with stroke

One of the main themes at the World Congress of Neurology 2001 is 'Stroke'. This issue carries an article on "Vascular Dementia" in which Prof. Vladimir Hachinski puts his views that a time has come for a new approach to this ever increasing cause of dementia in the elderly and that there is a need for it to be clearly delineated from dementia due to Alzheimer's disease, although both may co-exist in some patients. He has suggested that we need to overturn our current approach of gathering data into arbitrary, dogmatic, obsolete categories and begin developing a new pragmatic, systematic, data based approach. Congratulations to him, incidentally, for having been appointed Editor-in-Chief of the prestigious journal 'Stroke'.

Prof. Salvatore DiMauro has with great brevity discussed the intricate problems and concepts of "Mitochondrial Encephalopathies" which at one time were considered as myopathic ailments in children with mental dysfunction and renal derangement. Prof. DiMauro deserves our thanks for this explicit write up of a difficult problem.



*Jagjit S. Chopra, MD*  
Editor-in-Chief, World Neurology

and vascular dementia, both of which will assume leading positions, depending on the nation, as causes of disability and death by the year 2025. We in neurology must make a global plan for the field of stroke and, to that end, the International Stroke Society has chosen to have a Strategic Planning Retreat in London, immediately preceding the World Congress of Neurology, so that plans for a parallel relationship with the World Federation of Neurology can become a reality.

In February, I had the good fortune to be invited to address the National Institute of Neurology and Neurosurgery in Mexico City, on the occasion of its conclusion of the academic year. Director General Julio Sotelo presided at a most remarkable convocation (see photograph on

*(cont. on page 4)*

*(President's Column – cont. from p. 3)*

frontpage). Founder Emeritus Professor Velasco Suarez proudly informed me that he was the first neurosurgeon in Mexico. His efforts, and those of Dr. Francisco Rubio-Donnadieu, are now being taken up by Director General Julio Sotelo and his associates, Alfredo Gomez Avina, Misael Uribe, in collaboration with child neurologist Jose Eduardo San Esteban, the Deputy Minister of Health for Mexico. All of these individuals are extremely enthusiastic about the opportunities for equitable distribution of health care in Mexico. They have a very inclusive outlook for clinical neuroscience, which includes embracing their colleagues in psychiatry and neurosurgery, as well as other allied disciplines. One has the impression of a very vibrant organization, full of enthusiasm, under the direction of Dr. Teresa Corona, Teaching Director.

In April, my wife and I attended the Third Jordanian Neurosciences Society Conference, in collaboration with the Pan Arab Union of Neurological Societies, with endorsement by the World Federation of Neurology, in Amman, Jordan (see photograph above). Professor Ashraf Kurdi and Professor Abdel Karim Al-Qudah were the main organizers. Working with them in a very close relationship was the Organizing Committee, Scientific Program Committee, Social Committee, and the Finance Committee. All did enormous work in preparing a very exciting and successful program.

Thence, my wife and I went to Trest, Czech Republic, for the second EFNS European



*Dr. M. Zuheir Al-Kawi, Dr. Ashraf Kurdi, Dr. A. Kareem, Dr. Basim Yaqub*

Cooperation Neurology Workshop, with the purpose of bringing individuals from countries that do not ordinarily send delegates to World Congresses. It was most impressive to be with the young neurologists from Albania, Belarus, Bulgaria, Croatia, Czech Republic, Estonia, Georgia, Greece, Hungary, Moldova, Italy, Poland, Romania, Russia, Slovak Republic, Slovenia, Ukraine, and Yugoslavia. This, in my opinion, is one of the stellar accomplishments of the ten year old EFNS, the guiding lights of which have been Professor Franz Gerstenbrand and his wife, Friederike Tschabitscher, and now under the able leadership of Dr. Jes Olesen (see photograph below). They have been a

beacon shining to the East, encouraging young individuals from countries that do not have the opportunities that the developed countries have to learn the newest advances in the field of neurology and to become real participants in the neurosciences. These meetings are underwritten by the EFNS and serve as a model for other regional groups to emulate with the financial and intellectual support of the World Federation of Neurology. The EFNS is truly a regional model within neurological organizations and the WFN is proud to have encouraged this new development during the administration of Lord John Walton, Frank Clifford Rose, and Klaus Poeck. Another example of collaborative leadership also includes the combined efforts of the Association of British Neurologists and the EFNS with the World Federation of Neurology during this administration to effect a global meeting at the World Congress in London in June, which I hope the vast majority of neurologists in the world will attend, so that I can personally greet as many as possible. Hopefully, the EFNS will reach an accord with the ENS in the future, so that the scant resources available to neurology will not be duplicated unnecessarily.

We look forward to the election of new officers who will carry us into the future with the selection of the site of the next World Congress of Neurology, during the time of this upcoming Congress. There will be much excitement and many decisions in London. I hope that all who possibly can will attend.

*James F. Toole, MD*  
President, World Federation of Neurology



*European Federation of Neurological Societies Cooperation Workshop, Trest, Czech Republic - Professor Franz Gerstenbrand and Dr. Friederike Tschabitscher.*

## WFN COMMITTEE MEETINGS AT THE AAN

Dr Theodore Munsat chaired meetings of the Research Committee and Continuing Education Committee in Philadelphia during the recent annual meeting of the American Academy of Neurology. Attendance was not expected to be large, given that meetings of both committees will be held at the World Congress in London. Nevertheless, some useful issues were aired. After the London meeting of the Research Committee it is Dr Munsat's intention to distribute to Research Groups a list of funding organizations interested in support of international health groups. Under the new 'constitution' of the WFN (its so-called Articles of Association), the Research Committee will enjoy no special status as it did in the past and will become a Standing Committee like any other. Dr

Munsat's position as a trustee of the WFN continues to the end of 2001 but he holds it in a personal capacity. To assist in the process of selecting the next Research Committee Chair, suggestions were invited from those present and further consideration will be given to the matter in London. The Continuing Education Committee focused its attention on how best to use its limited resources and there was general support for directing efforts at neurology training programs. Lissette Jimenez from Puerto Rico undertook to work on a draft for a protocol to provide modest financial support for training programs in developing countries. This will contain methods of making the program known, reviewing requests and making awards.

## WFN TASK FORCE ON NEUROLOGICAL SERVICES

The Task Force on Neurological Services met in Philadelphia, Pennsylvania, USA, during the American Academy of Neurology's annual meeting. The Task Force has just completed a report for the WFN Management Committee on the global burden of neurological disease, and a survey on the number, training, and distribution of neurologists in WFN member countries. The report summarizes the tremendous toll on world health taken by neurodevelopmental disabilities and cognitive decline due to malnutrition and perinatal dis-

orders; stroke; brain and spinal injuries from road accidents, falls, self-injury, and war; neurological complications of HIV; and other neurological disorders. It also reveals the lack of reliable global health information available. The 'manpower' survey revealed that some countries have as few as one neurologist per million population, and that most neurologists work in large cities in private practice. Taken together, these reports identify a 'neurology gap' in many regions, in that the regions where most neurological disorders occur

## ADDITIONAL CANDIDATES FOR WFN ELECTIONS

The recommendations of the Nominating Committee for candidates for WFN positions were published in *World Neurology*, Volume 15 Number 4, December 2000. Under Article 6.3 of the WFN Articles of Association, any further nominations supported by 5 or more authorised Delegates and received by the Secretary-Treasurer General at least thirty days prior to the Annual General Meeting (Council of Delegates) are to be added to the list put forward for consideration.

The following two candidates will be added to the lists for the positions indicated:

Dr Antonio Culebras (USA)  
First Vice President

Professor Leontino Battistin (Italy)  
European Regional Vice President

are the very same ones where neurological expertise is lacking or unavailable. A summary of both of these projects will be presented at the WFN Congress in June.

*Donna C. Bergen*

Chair, WFN Task Force on Neurological Services

## ANNUAL REPORTS OF WFN RESEARCH GROUPS YEAR 2000

### Research Group on Neuroepidemiology (WFN-RGNE)

On March 5, 2000, the WFN-RGNE met in San Diego, CA at Forum Hall for its annual meeting. A total of 22 scientific

papers on a wide range of neuroepidemiologic topics were presented. An international group of neurologists and epidemiologists participated in representing many different countries. Dr. Friedland of San Diego delivered the keynote address. The meeting was organized and hosted by

Douglas Galasko, of the San Diego VA Medical Center. The Board meeting of the editors of the journal *Neuroepidemiology* took place prior to the WFN-RGNE meeting. Gustavo Roman, of the University of Texas Health Center in San Antonio was appointed as the new Editor-in-Chief replacing Dr. Philip Gorelick of Rush Presbyterian St. Luke's Medical Center. Dr. Alter will continue to serve as Editor Emeritus. Dr. Roman plans to make the journal a quarterly publication. While there is no official connection between the journal *Neuroepidemiology* and the WFN, that journal serves as a suitable medium for neuroepidemiologic publications. At the business meeting of the WFN-RGNE, it was decided to hold the next annual meeting again in conjunction with the AAN on Tuesday or Wednesday, May 8 or 9 in 2001 in Philadelphia. The meeting will be held in the

## WFN OFFICES BURGLIED

The building at 12 Chandos Street in London, where the WFN Secretariat is located and which it shares with two other organisations, was broken into during the night of 18/19 April. Computer equipment was stolen from all three offices and damage done to their doors and door frames. The WFN lost two computers, a printer, a scanner and a small amount of petty cash. More important, however, was the loss of data and files held on computer and it would be helpful to receive current e-mail and fax addresses, not only from Delegates and Committee Chairs and members but also others, such as Research Group Officers. We ask for your patience as we try to re-build our systems and procedures.

Keith Newton - Administrator

evening instead of at the beginning or the end of the week. The WFN-RGNE meeting will last 4 instead of 8 hours and posters as well as abstracts will be presented in order to accommodate 20 to 30 abstracts usually submitted. The meeting in Philadelphia will be hosted by Drs. Milton Alter and Gary Friday. The membership roster of the WFN-RGNE now includes approximately 600 names. It will be updated regularly. The RGNE will continue to charge a minimal registration fee to cover costs of lunch and coffee for the annual meeting. A nominating committee was appointed to elect the next President of the RGNE as the term of the current President, Dr. Milton Alter, will end in June 2001, at the next quadrennial meeting of the WFN in London, England. Dr. Walter Rocca and Dr. Gustavo Roman will serve on that committee.

*Dr. Milton Alter,*  
President, WFN-RGNE

## Research Group on the History of the Neurosciences

The Research Group on the History of the Neurosciences, one of the Research Groups of the World Federation of Neurology, is a forum for those who are interested in recording, exploring and publishing history. The Journal of the History of the Neurosciences, founded by Frank Clifford Rose as Founding Editor, is the official organ of this group (and also of the International Society of the History of the Neurosciences and of the European Club). The World Federation Group meets at each World Congress in order to present a series of papers. On the occasion of the World Congress of Neurology in London on Tuesday 19 June 2001 a session is devoted to the history of clinical diagnosis where five speakers will cover the structure and function of the nervous system as viewed over the ages, the reflexes, the concepts and description of disease, the examination of the patient and imaging. Platform presentations will deal with other historical topics. Members of the Research Group contribute to meetings worldwide and the group is pleased to include within its membership those interested in the history of the neurosciences who may wish to approach Christopher Gardner-Thorpe at [cgardnerthorpe@doctors.org.uk](mailto:cgardnerthorpe@doctors.org.uk) or by fax to + 44 1392 402721

The European Federation of Neurological Societies (EFNS) panel on the History of Neurology meets at each EFNS Con-

ference and provides a forum for those closer to Europe to promote the history of neuroscience in general and neurology in particular. It may be that a more clearly local flavour will be introduced into those meetings with discussion of neurohistory matters related to the city in which the meeting takes place but the work of the panel is wide-ranging. For further details please also approach Christopher Gardner-Thorpe at the e-mail or fax numbers given above.

*Christopher Gardner-Thorpe*

## Autonomic Disorders Research Group 2000 Annual report

Horacio Kaufmann, Eduardo Benaroch, Roy Freeman, Pietro Cortelli and Chris Mathias have organized scientific activities related to the autonomic nervous system that will take place at the XVII World Congress of Neurology in London. There will be a Scientific Symposium and an Educational Symposium to update general neurologists on new developments in the autonomic field.

Work is ongoing on a project studying possible involvement of the autonomic nervous system in the Cuban epidemic neuropathy. Forty-five patients have been studied to date. This is a joint project between the Instituto de Neurologia y Neurocirugía de La Habana, Cuba, Mt. Sinai School of Medicine and Harvard Medical School. Dr. Joel Gutierrez, Director of Neurophysiology at the Cuban Institute spent three months from March to May 2000 at Dr Kaufmann's laboratory in New York to complete the analysis of collected data.

The Research Group has been discussing several initiatives, including sponsoring a consensus conference on the diagnostic criteria of pure autonomic failure. Funding sources are still being explored.

Our funds are held in an account at Mount Sinai School of Medicine under the WFN name.

*Horacio Kaufmann, M.D.*  
Chairman Autonomic Disorders  
Research Group

## CSF Research Group

The development of a network on the Internet has been pursued during the year 2000. Interactive communications are restricted to some members of the group in order to obtain consensus about control quality and standardization of CSF

analysis. However, we started a Web-site open to everybody ([www.teamspace.net/csf](http://www.teamspace.net/csf)) where consensus and typical profiles of CSF abnormalities will be presented in the near future. One face-to-face meeting of the Consensus Group was organized in Göttingen on May 18th-20th, 2000 by Prof. H. Reiber.

Another international meeting was held in Marburg on September 29th-30th, with the support of the CSF Research Group. This meeting, organized by Professor Kleine, was entitled "European CSF Symposium on Laboratory Diagnosis of Human Brain Injury and Inflammation" and was attended by 80 participants.

## Neurotoxicology Research Group Annual Report 2000

The Neurotoxicology Research Group (NRG) was added to the list of Research Groups of the World Federation of Neurology in 1999; Dr. Robert G. Feldman was introduced as its first Chairman by Dr. Ted Munsat, Chairman of the Research Committee, at the meeting held at the Hyatt Regency Hotel in San Diego, California on May 2, 2000.

## Defining a Mission

Dr. Robert G. Feldman consulted with WFN President, Dr. James Toole immediately after the meeting in San Diego to learn more about the WFN and to benefit from his experience. At another meeting, held later during the year in Boston, Dr. Munsat and Dr. Feldman reviewed the policies and procedures necessary for organizing a new Research Group. The successes and pitfalls of previous committee programs were discussed. It was decided that the mission of the new Neurotoxicology Research Group would focus on topics of Neurotoxicology as they relate to Occupational and Environmental Exposures to chemicals, encountered by people throughout the world. Special attention would be directed towards educational and research programs dealing with conditions and problems that exist in newly emerging and industrializing nations. Efforts would be made to bring resources and expertise from established academic centers to communities in need and desirous of developing educational materials, programs, and research opportunities. It is hoped these will lead to a better appreciation of the risks of exposure to various man made chemicals and/or biologically available substances that can alter the structures and functions of the nervous system.

## Inviting Participation of Interested Persons

An informational letter from the Chairman was sent to an initial group of 35 individuals who were selected from the membership list of the American Academy of Neurology and from a list of names recognizable to Dr Feldman as having contributed to the fields of neurotoxicology, and occupational and

environmental medicine. These people were invited to attend the organizational meeting of the NRG on Wednesday, June 20, 2001 from 08.00 to 09.30 in London during the World Congress of Neurology. A room has been booked and responses have already been received from several persons who plan to attend and from others who hope to participate in the Group in future.

## Funding Sources

Possible sources of funding to help organize the setting up of the Group include the Federation of American Societies for Experimental Biology (FASEB) (MARC Program Activities); the British Ecological Society; and Biological Databases and Informatics.

## ACUTE STROKE UNITS IN AUSTRIA

Since 1997 stroke units have been established in Austria to function as a nationwide network for acute stroke treatment. At present some 25 units are functional and this number is expected to double by 2005 to form a complete network for the country's 8 million inhabitants. The Austrian health authorities have commissioned a plan that has the following specifics: 1) Stroke units are exclusively set up in neurological departments. 2) Isochrones (time for ambulances to cover any given distance to the nearest stroke unit) should not exceed 90 minutes from any community in the country. 3) Stroke units have a predefined structure quality and this quality is controlled by the regional health authorities. 4) Reimbursement for "acute stroke treatment" is allocated to hospitals only for patients treated within stroke units.

To acknowledge this ambitious achievement it is necessary to comprehend that Austria's health system is almost completely state controlled. Due to a general health insurance that is obligatory (a private one can be held additionally) social or class differences for the availability of such a health care system are negligible. It has been possible to set up a central plan for acute stroke units as well as for additional neurological beds for early rehabilitation that are assigned either to the same neurological department or to a neurological department within the region of the stroke unit. These rehabilitation beds are financed separately. They are defined either by additional nursing needs (1.5 nurses per bed) or by intensive rehabilitation programmes (at least 3 hours of rehabilitation per day).

The structure quality for an acute stroke

unit in Austria includes a defined and closed region of 4–8 beds that are exclusively dedicated for acute stroke patients. This unit requests the leadership of a neurologist, a board certified neurologist must be present 24 hours, an internist must be available (present or on call) 24 hours, at least 1 nurse is assigned per bed, one physiotherapist, one occupational therapist and one speech therapist must be assigned to the unit, continuous monitoring of vital parameters (ECG, breathing pattern, pulse rate, blood pressure, oxygen saturation), CT immediately available 24 hours (MRI available during the day hours), availability of Duplex sonography and transcranial Doppler sonography within the department, arteriography (reachable within 30 minutes), neurosurgery (reachable within 30 minutes), intensive care ward available within the same hospital.

An evaluation of the process quality of 15 stroke units within the year 2000 has shown that these units have in the meantime become well accepted by the medical emergency system as well as by the general public. A prospective documentation of more than 2,000 acute stroke patients treated in these stroke units has shown that 30% of all cases are admitted within 120 minutes after stroke onset, 50% of all cases have an emergency CT within 30 minutes after their admission, and 4% of all patients undergo thrombolysis. 20% of all patients had severe strokes, in addition the proportion of haemorrhages was 10%, and in total more than 5% were soporous or in coma. The average stay within the unit was 3–5 days and mortality was 12%. This shows that these units fulfil all the functions for all cases of stroke and do not only accept the prognostically

favourable cases. This system does not aim at treating all incident strokes but only some 60–70 percent by 2005. Other cases of stroke are treated within general medical departments (varying by region). Mostly these are cases that have a more pronounced prestroke disability and thus a higher probability of multimorbidity. It is important not to draw a line set by age alone, as there is no scientific evidence that favours triage by age criteria alone. Rather, a higher probability of multimorbidity (as is also reflected by many cases with high age) tends to be treated primarily in medical wards. These medical wards are motivated to set up mobile stroke teams where neurologists also participate but need not be available 24 hours (as is the case in many rural areas).

The total number of some 500 board certified neurologists in Austria can cope with this workload. This plan of action has also led to the establishment of new neurological departments and to the growing recognition of neurologists to participate in emergency medicine.



*Prof. Michael Brainin, MD*  
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## PAN-ARAB UNION OF NEUROLOGICAL SCIENCES

### History and Update

The Pan-Arab Union of Neurological Sciences (PAUNS) was founded through the inspiration of Arab neurologists who attended the World Federation Neurology

Meeting in Barcelona, Spain, in 1973. This inspiration came into reality in 1975 when the Egyptian Society of Neurology, Neurosurgery and Psychiatry called for its first meeting in Cairo, Egypt. Dr. Yahya Taher was elected as President of the Confer-

ence and the late Dr. Ahmad Al Banhal as Secretary. This meeting was attended by Dr. Jamal Al Din Behairi, Secretary-General for the Pan-Arab Physicians. The delegates who attended from the different Arab countries were: Immaddin Farid



Opening ceremony during the 8th PAUNS Conference in Beirut, Lebanon (April 13–16, 2000) attended by His Excellency Dr. Karam Karam, Minister of Public Health, and Dr. Sohail Gebeily, President of the Lebanese Neurological Society.

(Bahrain), Mohammad Abadu (Algeria), Ashraf Al-Kurdi (Jordan), Daoud Mustafa (Sudan), Tariq Hamdi (Iraq), Sohail M. Saleh (Kuwait), Abdul Rahman Al-Wazzazi (Morocco), Baltayeb Abdul Karim (Tunisia), Faisal Al-Sabag (Syria), Foud Hadad (Lebanon), and Yehya Taher (Egypt).

Dr. Ahmed Al Banhawi was elected as the first Secretary-General for the PAUNS. Assistants to the Secretary-General were Dr. Tariq Hamdi (Iraq), Dr. Mohamed Emad Al-Deen Fadli (Egypt), and Dr. Jamal Assaf (Egypt). Mr. Abdulhakim Al Marsafawi was elected as Treasurer. Dr. Sayed Al Jindi was elected to be the Representative of the PAUNS to the Arab European Society for Neurosciences. After the establishment of the PAUNS, several meetings were conducted, though it was not regular.

The second meeting was in Tunisia (1978), and the third was in Jordan (1984).

Dr. Ashraf Al-Kurdi was elected in 1984 as the Secretary-General. The fourth meeting was convened in Algeria (1986), and the fifth meeting was held in Tunis (1993). Dr. Mohamed Emad Al-Deen Fadli was elected as Secretary-General in Tunisia (1993). The sixth meeting was held in Egypt (1995), and the seventh meeting was conducted in Saudi Arabia (1997). Dr. Saleh M. Al Deeb was elected as Secretary-General in Riyadh (1997). Later, the title of Secretary-General was changed to be recognized as President of PAUNS. During the 7th meeting, an extensive program has been done with faculties worldwide. Also, in this Conference, the 1st PanArab Epilepsy Conference was held

followed by a one-day Tropical Neurology Conference. This meeting was a success and attended by more than 400 members. The last meeting was conducted in Beirut, Lebanon, on 13-16 April 2000, and was held under the patronage of His Excellency, Dr. Karam Karam, Minister of Public Health, who gave the opening remarks. Prof. Samir Atweh, Head of Neurology, American University of Beirut, was the President of the Conference, and the number of attendees was around 500. Many papers were submitted and several workshops were conducted, and the Conference was a great success. Also, regional neurological symposia in different Arab countries were held successfully under the auspices of PAUNS.

As neuroscience has been expanding in the Arab world, a few important societies have been established through the Pan-Arab. In 1994, the Pan-Arab Neurological Society was formed, and Dr. Mohamed Aabed Al Thagafi is the current President. Also, the Arab Neurological Society was formed in December 1995, and Dr. Khalaf Al Moutaery was elected as the President. As a member of the WFN, we have revised the Constitution of the PAUNS, and as it stands, it has been amended and agreed by the majority of the members. There are many tasks to achieve, and we are planning to have a proper established constitution for the PAUNS. This cannot be done without the cooperation of all the members.

*Saleh M. Al Deeb,*  
President, PAUNS, Riyadh Armed Forces Hospital, Box 7897, Riyadh 11159, Saudi Arabia; E-mail: rkhnksa@zajil.net

## WINNERS OF 2001 JUNIOR TRAVELLING FELLOWSHIPS

Name	Country	Meeting
1. Dr M.A. Alleem	India	XVII World Congress of Neurology, London
2. Dr Manvir Bhatia	India	48th Annual Meeting of American Academy of Electrodiagnostic Medicine, New Mexico
3. Dr A. Nalini	India	XVII World Congress of Neurology, London
4. Dr Pramod Kumar Pal	India	XVII World Congress of Neurology, London
5. Dr Jeyaral Pandian	India	XVII World Congress of Neurology, London
6. Dr Atul Prasad	India	XVII World Congress of Neurology, London
7. Dr Nazha Birouk	Morocco	XVII World Congress of Neurology, London
8. Dr George Kuchukhidze	Georgia	XVII World Congress of Neurology, London
9. Dr Zdenek Novotny	Czech Republic	XVII World Congress of Neurology, London
10. Dr Paul Pasco	Philippines	XVII World Congress of Neurology, London
11. Dr Seyam Saed	Egypt	XVII World Congress of Neurology, London



## WFN JUNIOR TRAVELLING FELLOWSHIP REPORTS

I am very thankful to the World Federation of Neurology that had permitted me thanks to its award to participate in the 125th Congress of the American Association of Neurology held in Boston, 15–20 October 2000.

This event allowed me an update on most neurological fields, particularly on cerebrovascular diseases and cognitive disorders that constituted for me particular topics of interest.

It had also provided me the opportunity to discuss with neurologists from all over the world and to exchange with them ideas concerning recent and important progress of neurology in the domain of basic sciences and therapy. Gene therapy sounds very promising in numerous neurological diseases.

I noticed the exceptional quality of interventions during the presidential symposium that analyzed the relationship between conscience, behaviour and emotion in light of the new data of the neuro-

imagery and neurobiology.

We are very grateful to the WFN for enabling neurologists from developing countries to benefit from recent research in different domains of neurology.

*Dr Ibtissem Ben Hamouda*  
Tunisia

I was delighted to win a WFN – Glaxo Wellcome Junior Travelling Fellowship to attend the 4th World Stroke Congress in Melbourne, Australia, in November 2000. The Congress was a great experience. I had the privilege to listen to, and share experiences with, many neurologists and stroke physicians, including some of the leading experts in the field. The scientific sessions dealt with many a new advance at the cutting edge of stroke medicine. I was glad to be given the opportunity to present two papers on our experience of stroke care in Sri Lanka at the Congress. The best moment of all was when I won a “Young Investigator of the Year” award;

that was the icing on the cake.

The Travelling Fellowship also helped me attend the 6th International Symposium on Acute Stroke and Thrombolytic Therapy held in Hamilton Island immediately after the World Stroke Congress. I am sure the experiences I have gained participating in these two conferences would help me contribute towards improving the stroke services in my country.

This was my first visit to Australia, and I took the opportunity to do as much ‘sight seeing’ as possible within the limited time. Watching the koalas and kangaroos at the Healesville sanctuary, snorkeling at the Great Barrier Reef, and marvelling at the Penguin Parade on the Philip Island beach are some of the memories I will cherish for a long time.

Thank you, WFN and Glaxo Wellcome, for a wonderful experience.

*Udaya K. Ranawaka*  
Sri Lanka

## FIRST LACTRIMS CONGRESS

Several years ago a group of Latin-American visionaries interested in one of the more chronic, crippling and challenging diseases decided to combine their efforts to found LACTRIMS (Latin American Committee for the Treatment and Research in Multiple Sclerosis) to research the real state of Multiple Sclerosis in our countries and to explore comparisons with North-American and European knowledge in order to benefit our neurologists and their patients and families.

The official foundation of LACTRIMS was in Cartagena de Indias, Colombia, during the X Pan-American Congress of Neurology in October 1999 where the General Assembly elected Dr. Leonor Gold (Argentina) as President, Dr. Victor Rivem (Mexico) as Vice-President, Dr. Edgardo Cristiano (Argentina) as General Secretary, Dr. Marco Lana Peixoto (Brazil) as Treasurer, and Drs. Carlos Oehninger (Uruguay), Jorge Luis Sánchez (Colombia) and Dr. José Antonio Cabrera Gómez (Cuba) as Vocals. Also, the Committee approved the organization of the 1st LACTRIMS Con-

gress to be held in Buenos Aires the following year.

From 9 to 11 November 2000, more than 300 neurologists and scientists from related disciplines gathered with great enthusiasm to attend this international meeting in the beautiful city of Buenos Aires. The Organizing Committee was chaired by the dynamic Dr. Leonor Gold with the assistance of Dr. Edgardo Cristiano as Vice-President, Dr. Marco Lana Peixoto as Treasurer and several neurologists from different Latin-American countries.

There were 44 speakers from Argentina, Brazil, Canada, Chile, Colombia, Cuba, Italy, Mexico, Peru, Switzerland, United Kingdom, Uruguay, USA, and Venezuela. The themes included Epidemiology in Latin America, Natural History, Diagnostic Criteria and Clinical Forms, Role of Imagenology, Complementary Tools, Cognitive Impairment, MS Centers, MS in Childhood, MS and Pregnancy, Assessment Scales, Treatment, and a special session dedicated to patients and their families.

Also, there were 97 posters from Argentina, Brazil, Canada, Colombia, Cuba, Spain, Israel, Mexico, Panama, Puerto Rico, Switzerland, Uruguay, USA, and Venezuela.

The meticulous organization, the modern and comfortable settings, the high level of the scientific sessions and the warm and gentle friendship made for a successful 1st LACTRIMS Congress.

The farewell dinner was in “Senor Tango” an amazing temple dedicated to the two Argentinean traditions: the dance and the delicious meat, and everybody enjoyed them very much. All the participants were agreed that we must recommend to our MS patients to dance the tango as one of the rehabilitation strategies!

Dr. Victor Rivera, as President, will organize the 2nd LACTRIMS Congress in Mexico, in 2002, and we can be sure of its success.

*Dr. Gustavo Pradilla*  
Bucaramanga, Colombia

## VASCULAR DEMENTIA: IT IS TIME FOR A NEW APPROACH

Current concepts of vascular dementia are obsolete. Conventional definitions identify the patients too late, miss subjects with cognitive impairment short of dementia, and emphasize consequences rather than causes, the true bases for treatment and prevention.

### Obsolescence of current concepts of vascular dementia

For each patient considered demented, there is another individual with cognitive

impairment short of dementia (CIND). The cornerstone of all criteria of dementia is memory impairment. This criterion works very well for Alzheimer’s disease, where memory is an early and constant feature, but it seldom helps in identifying individuals with cognitive impairment on a vascu-

lar basis. About 80% of all strokes occur in the carotid artery distribution, only 20% affecting the vertebrobasilar system, which supplies the hippocampi. While strokes in the medial temporal lobes cause memory impairment, it usually takes bilateral lesions to cause serious and permanent memory problems. Strokes affecting cognition occur most commonly in the fronto-basal systems that subserve judgement, planning and emotion, features seldom tested in cognitive screens. The most fundamental problem with current criteria of dementia is that they do not work. In the Canadian study of Health and Aging, which is both a population and institution based study, 1879 subjects were identified as demented by consensus. Then six commonly used criteria of dementia were applied to the same subjects. Little overlap emerged, and a surprising 10-fold difference separated the least and the most sensitive criteria. According to ICD-10 criteria, 3.1% of the population over the age of 65 years are demented, by DSM-III criteria 29.1% are!

### Ascertainment and classification biases

Most clinicopathological studies are carried out on patients who have been identified through memory or Alzheimer clinics. Since they come to attention because of memory problems, most of them will turn out to have Alzheimer's disease. By contrast, patients with cerebrovascular disease usually come to medical attention because they have had transient ischemic attacks or strokes. If these patients have cognitive impairment, it is often frontal lobe dysfunction, which is difficult to diagnose and test. Even if identified, these patients seldom find their way into clinicopathological studies of dementia because the current definitions of dementia require memory impairment as the first requisite, and memory is seldom severely impaired in patients with cerebrovascular disease. Thus there is a systematic overrepresentation of Alzheimer cases in clinicopathological series. This is compounded by another phenomenon. Most clinicopathological studies claim an accuracy of about 90% in the diagnosis of Alzheimer's disease. However, only patients who die come to autopsy, typically 7–8 years after diagnosis in Alzheimer's disease. If one includes in the denominator the 23% of patients who initially are diagnosed as Alzheimer's disease who do not deteriorate cognitively and survive, the accuracy drops to about two-thirds.

## FELLOWSHIP TRAINING PROGRAM IN NEUROPSYCHIATRY

The Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez (National Institute of Neurology and Neurosurgery) in Mexico City is opening a Fellowship training program in Neuropsychiatry, a field that tries to understand the complex inter-relationships between human behaviour and brain function by incorporating the areas of psychiatry and neurology. Over the past several years, there has been an increasing interest in neuropsychiatry as a sub-specialty which focuses on the applications of insights from basic and clinical neuroscience research to the study of psychopathology.

The fellowship is directed at neurologists and psychiatrists. It is a one year long training program, oriented not only towards research activities but also to clinical evaluation and treatment. For more information, please contact Dr. Ignacio Ruiz-López: Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez Insurgentes Sur 3877, C.P. 14269, México, D.F. Phone number and fax: (52) 56064532; e-mail: iruizl@yahoo.com.

### From multi-infarct dementia to vascular cognitive impairment

We suggested the term "multi-infarct dementia" to emphasize that when dementia occurs on a vascular basis, it is usually due to multiple infarcts and not to the slow strangulation of the brain's blood supply resulting in chronic cerebral ischemia and neuronal starvation and death. While multi-infarct dementia occurs, it is rare in pure form. What is much more common is cognitive impairment on a vascular basis short of dementia. Thus, Bowler and I have suggested the term "vascular cognitive impairment" to describe the spectrum of cognitive impairment on a vascular basis, from mild impairment to frank dementia. The commonest context of multi-infarct dementia occurring in patients with Alzheimer changes i.e. "mixed dementia". The "ischemic score" distinguishes very well pure Alzheimer's disease from multi-infarct and mixed dementia but not between the latter two. This does not matter pragmatically, the important point being the identification of the treatable vascular component.

### Leukoaraiosis

We coined the term "leukoaraiosis" to describe white matter rarefaction as seen on brain imaging and to emphasize that although ischemia is often invoked as the cause, white matter changes may be due to multiple causes. While white matter changes can occur in the elderly without any clinical correlates, consistent associations have been described between periventricular white matter changes and cognition. Subcortical white matter changes may be accompanied by depression. Leukoaraiosis is associated with an increased

risk of stroke, vascular death, cognitive deterioration and with a 3–4-fold increased risk of intracerebral bleeding in patients placed on anticoagulants.

### Co-existence and possible interaction for stroke and Alzheimer's disease

Snowden et al have shown that among elderly nuns having the pathological diagnosis of Alzheimer's disease only 57% were demented. Among those having the pathological diagnosis of Alzheimer's disease plus cortical infarcts 75% were demented and among those having pathological Alzheimer's disease and small infarcts in the subcortical areas, 93% were demented. Clearly the effects of Alzheimer's disease and strokes add up or perhaps interact, since lesions in the brain do not add up, they multiply. In a clinical pathological study addressing the question of education and dementia, no difference was found in the progression of dementia once diagnosed, among individuals with a primary education, secondary education and college or university education. Similarly, the degree of brain atrophy, presence of senile plaques and neurofibrillary tangles was comparable among the educational groups. However, the least educated patients had significantly higher prevalence of lacunar infarcts, white matter lesions, macroscopic infarcts and other vascular lesions than the other two groups with higher education.

### The need for a new approach

We need to take a pragmatic conceptual

retreat before we are ready to advance at an accelerated pace. We need to identify potential patients long before they are demented, including symptomless individuals at high risk of developing cognitive impairment. When subjects have cognitive impairment, this should be characterized clinically and by a commonly agreed minimum of standardized tests. We may have to make an initial diagnosis of a "cognitive syndrome" and become more precise as the data allow.

## Conclusion

We should abandon current diagnostic categories and describe cognitive impairment clinically and according to commonly agreed instruments that document the demographic data in a standardized manner and undertake a systematic effort of identifying the underlying etiology in each case. Imaging and DNA should be obtained whenever possible. An empiric approach and the use of mutually intelligible descriptions will contribute to a knowledge base that will increase not only our

understanding, but will give us the basis for therapy. Already, enough scientific rationale exists for undertaking systematic clinical trials in the prevention of cognitive impairment through the control of vascular risk factors and the use of statins, anti-inflammatory agents and ACE inhibitors. We need to overturn our current approach of gathering data into arbitrary, dogmatic, obsolete categories and begin developing a new pragmatic, systematic, data based approach.



Vladimir Hachinski, M.D., FRCP(c), D.Sc.,  
Chair, Steering Committee and WFN Vice-  
President for North America

Dr. Hachinski has been named Editor-in-Chief of the journal *Stroke*. This American Heart Association (AHA) publication is the leading scientific journal in the field. Dr. Hachinski had previously been chair of the Scientific Programme Committee of the annual International Stroke Conference of the AHA, the only person to hold both positions. His contributions include pioneering with Dr. John W. Norris the establishment of stroke units, subsequently proven to improve morbidity and mortality of stroke patients, discovering the key role of the insula of the brain in cardiac complications of stroke including sudden death, crystallizing the concepts and coining the terms "multi-infarct dementia", "leuko-araiosis" and "brain attack" and devising the "ischemic score" that bears his name. The headquarters of the journal have been moved to London, Ontario and Dr. Hachinski has also established associate editors' offices at the University of Helsinki, Finland, the Royal Perth Hospital, Australia, and Harvard University, U.S.A.

## MITOCHONDRIAL ENCEPHALOMYOPATHIES

Mitochondrial myopathies have been known since the early 1960s, when systematic ultrastructural and histochemical studies, pioneered by G. Milton Shy, Nicholas Gonatas, and W. King Engel, revealed excessive proliferation of normal- or abnormal-looking mitochondria in muscle of patients with weakness or exercise intolerance. Because, with the modified Gomori trichrome stain, the areas of mitochondrial accumulation looked like purplish blotches, the abnormal fibers were dubbed "ragged-red fibers" (RRF) and came to be considered the pathological hallmark of mitochondrial disease. The

first biochemical documentation of mitochondrial dysfunction was provided by Professor Rolf Luft and coworkers in a patient with exercise intolerance, RRF, and nonthyroidal hypermetabolism due to "loose coupling" of muscle mitochondria. It soon became apparent, especially to pediatric neurologists, that in many patients with RRF, the myopathy was overshadowed by diverse symptoms and signs of brain involvement, and the term *mitochondrial encephalomyopathies* was introduced. While this label correctly highlights the special vulnerability of brain and muscle to defects of oxidative me-

tabolism, it is unduly restrictive in that mitochondrial diseases, and especially those due to defects in mitochondrial DNA (mtDNA), can affect any tissue in the body and often cause protean multisystem disorders.

In 1988, the era of *mitochondrial genetics* was ushered in by two seminal papers, one from the group of Anita Harding, the other from the group of Douglas Wallace, describing the first pathogenic mutations in human mtDNA. Human mtDNA is a 16.5-kb circular, double-stranded molecule, which contains 37 genes: 2 rRNA genes, 22 tRNA genes, and 13 structural genes encoding subunits of four complexes of the respiratory chain (7 subunits of complex I; 1 subunit of complex III, 3 subunits of complex IV; and 2 subunits of complex V). According to the widely accepted "endosymbiotic hypothesis", mitochondria are the remnants of protobacteria that populated anaerobic nucleated cells and endowed them with the precious gift of oxidative metabolism. This explains how eukaryotic cells are "genetic mosaics", containing their own nuclear genome (nDNA) plus multiple mitochondrial genomes. This scenario helps explain the central concepts of mitochondrial genetics:

(i) *Heteroplasmy* and the *threshold effect*. Each cell contains hundreds or thousands

## INTERNATIONAL FEDERATION OF MULTIPLE SCLEROSIS

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of mtDNA copies, which, at cell division, distribute randomly among daughter cells. In normal tissues, all mtDNA molecules are identical (homoplasmy). Deleterious mutations of mtDNA usually affect some but not all mtDNAs within a cell, a tissue, an individual (heteroplasmy), and the clinical expression of a pathogenic mtDNA mutation is largely determined by the relative proportion of normal and mutant genomes in different tissues. A minimum critical number of mutant mtDNAs is required to cause mitochondrial dysfunction in a particular tissue. (ii) *Mitotic segregation*. At cell division, the proportion of mutant mtDNAs in daughter cells may shift and the phenotype may change accordingly. This phenomenon, called mitotic segregation, explains how certain patients with mtDNA-related disorders may actually shift from one clinical phenotype to another as they grow older. (iii) *Maternal inheritance*. At fertilization, all mtDNA derives from the oocyte. Therefore, the mode of transmission of mtDNA and of mtDNA point mutations (single deletions of mtDNA are usually sporadic events) differs from mendelian inheritance. A mother carrying a mtDNA point mutation will pass it on to all her children (males and females), but only her daughters will transmit it to their progeny. A disease expressed in both sexes but with no evidence of paternal transmission is strongly suggestive of a mtDNA point mutation. The best way for the clinician to chart her course toward a diagnosis in the *mare magnum* of mitochondrial encephalomyopathies is to use a classification that combines genetic and biochemical criteria. However, by a generally accepted convention, the term "mitochondrial encephalomyopathies" is now restricted to defects of the respiratory chain. Because of the dual genetic control of the respiratory chain, these disorders will be due either to mutations in mtDNA or to mutations in nDNA.

## 1. Disorders due to defects of mtDNA

These include rearrangements (single deletions or duplications) and point mutations.

### A. mtDNA rearrangements

Single deletions of mtDNA have been associated with three sporadic conditions: (i) Pearson syndrome, a usually fatal disorder of infancy characterized by sideroblastic anemia and exocrine pancreas dysfunction. (ii) Kearns-Sayre syndrome (KSS), a multisystem disorder with onset before age 20 of PEO, pigmentary retinopathy,

and heart block. Frequent additional signs include ataxia, dementia, endocrine problems (diabetes mellitus, hypoparathyroidism). (iii) PEO with or without proximal limb weakness, often compatible with a normal lifespan. Deletions vary in size and location, but a "common" deletion of 5 kb is frequently seen in patients and in aged individuals. Duplication of mtDNA can occur in isolation or together with single deletions and have been seen in patients with KSS or with diabetes mellitus and deafness. Duplications and duplications/deletions are transmitted by maternal inheritance.

### B. Point mutations

Over 100 pathogenic point mutations have been identified in mtDNA from patients with a variety of usually maternally-inherited and usually multisystemic disorders. Among the encephalomyopathies, common syndromes include: (i) MELAS (mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes), presenting usually in childhood with recurrent vomiting, migrainelike headache, and strokelike episodes causing cortical blindness, hemiparesis, or hemianopia. CT scan or MRI of the brain shows "infarcts" that do not correspond to the distribution of major vessels, raising the question of whether the strokes are vascular or metabolic in nature. The most common mtDNA mutation associated with MELAS is A3243G in the tRNA<sup>Leu(UUR)</sup> gene. (ii) MERRF (myoclonus epilepsy with ragged red fibers) is characterized by myoclonus, seizures, mitochondrial myopathy, and cerebellar ataxia. Less common signs include dementia, hearing loss, peripheral neuropathy, and multiple lipomatosis. The typical mtDNA mutation in MERRF is A8344G in the tRNA<sup>Lys</sup> gene. (iii) NARP (neuropathy, ataxia, retinitis pigmentosa) usually affects young adults and causes retinitis pigmentosa, dementia, seizures, ataxia, proximal weakness, and sensory neuropathy. This syndrome is associated with a mutation (T8993G) in the ATPase6 gene of mtDNA. When the same mutation is present in high abundance, it causes a more severe infantile encephalopathy with the neuropathological features of Leigh syndrome. (iv) LHON (Leber's hereditary optic neuropathy) is characterized by acute or subacute loss of vision in young adults, more frequently males, due to bilateral optic atrophy. Several different mtDNA point mutations in structural genes (mostly genes encoding subunits of complex I) have been associated with LHON, but only a few are exclusively present in patients and appear to be pathogenic even when present in isolation

(primary mutations).

While exercise intolerance is a common complaint in patients with mitochondrial encephalomyopathies, it is often overshadowed by other symptoms and signs. Only recently we have come to appreciate that exercise intolerance, myalgia, and myoglobinuria can be the sole presentation of respiratory chain defects. These are due to mutations in mtDNA genes encoding subunits of complex I, complex IV, or, more frequently, cytochrome *b*. As these disorders are usually tissue-specific and sporadic, they are apparent exceptions to the "common wisdom" that mtDNA point mutations are invariably associated with multisystemic, maternally-inherited conditions.

## 2. Disorders due to defects of nDNA

These are all transmitted by mendelian inheritance and include two major subgroups.

### A. Mutations in genes encoding respiratory chain subunits or "ancillary proteins"

As pathogenic mutations start to overcrowd the small circle of mtDNA, searching for deleterious mutations in nuclear genes controlling respiratory chain complexes has become the "new frontier" of research in mitochondrial diseases. Several mutations have already been identified in genes encoding subunits of complex I and complex II, mostly in children with Leigh syndrome. The situation is more complex (and more interesting) in patients with complex IV (cytochrome *c* oxidase, COX) deficiency. Mutations have not been found in nuclear genes encoding COX subunits, but, rather, in genes encoding COX-assembly proteins, a sort of "murder by proxy" situation. Already four such ancillary proteins have been involved, again mostly in children with Leigh syndrome, and more are undoubtedly "waiting in the wings".

### B. Defects of intergenomic signaling

As mentioned above, mtDNA is highly dependent for its proper function and replication on numerous factors encoded by nuclear genes. Mutations in these genes cause mendelian disorders characterized by qualitative or quantitative alterations of mtDNA. Examples of qualitative alterations include autosomal dominant or autosomal recessive *multiple deletions of*

*mtDNA*, usually accompanied clinically by progressive external ophthalmoplegia (PEO) plus a variety of other symptoms and signs. Two genes responsible for multiple *mtDNA* deletions have been identified. Mutations in one (encoding the enzyme thymidine phosphorylase) are associated with an autosomal recessive syndrome known as MNGIE (mitochondrial neurogastrointestinal encephalomyopathy). Mutations in the other (encoding an adenine nucleotide transporter, ANT1) are associated with autosomal dominant PEO. Examples of quantitative alterations of *mtDNA* include severe or partial expressions of *mtDNA depletion*, usually characterized clinically by congenital or childhood forms of myopathy or hepatopathy. The mutant gene (or genes) and factors associated with *mtDNA* depletion remain unknown.



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New York, NY, USA

## BOOK REVIEWS

### Central Nervous System Angiitis

Editor : Schmidley, J.W.  
ISBN : 0 7506 7153 X  
No. of pages : 216  
Price : £55.00  
Publication Date : 2000  
Publisher : Butterworth Heinemann

There have been few, if any, comprehensive works covering the various aspects of central nervous system angiitis. This monograph is therefore welcome. It is small well updated to 1998 and has 578 literary references. Apparently, the book is written as an argument against the 'widespread misconceptions concerning angiitis and the central nervous system' such as 'the widespread, groundless belief that the central nervous system manifestations of systemic lupus erythematosus are caused by angiitis and an entirely misplaced confidence in catheter angiography as a sensitive and specific means

of diagnosis'. It is indeed well done. The author has collected data on clinical manifestations of CNS angiitis both from numerous reports as well as from his own material. The author covers thoroughly giant cell arteritis, Takayasu's arteritis, polyarteritis nodosa and the CNS involvement in systemic lupus erythematosus as well as many other conditions. There are special chapters on CNS angiitis due to infection and CNS angiitis associated with drug abuse. The book is written in a fluent, sometimes epic style ("Behçet's disease is a mysterious disorder." or "I hold little hope that newer imaging techniques such as functional MRI, PET or NMR angiography will be helpful in sorting out this confusing clinical problem"). He argues strongly that cerebral angiography is of little value in the diagnosis of CNS angiitis. There is, however, only one illustration showing angiographic changes (possibly mis-) interpreted as showing angiitis, but with too few details to be convincing. The chapters on cerebrospinal fluid analyses and of immunology are less informative. The strengths of the book are the detailed description of various forms and symptomatology of CNS angiitis, the discussion of the value of leptomeningeal biopsy and the documentation of the effect of immuno-suppression.

Dr. Johan Aarli  
Bergen, Norway

### The Nervous System and the Heart

Ed : Gert J Ter Horst  
ISBN : 0 89603 693 6  
No. of pages : 564  
Price : US\$135.00  
Publication Date : 2000  
Publisher : Humana Press

This interesting book on the association between the heart and the nervous system is nicely edited by Gert Ter Horst. It consists of 5 parts and 13 sub-topics. The main themes are autonomic control, the hypothalamus pituitary adrenal system and the heart, heart pain, the neuroanatomy of cardiac nociceptive pathways, humoral factors, and finally heart disease and brain dysfunction. The book covers basic physiological, anatomical and its clinical implications, and explains very nicely many symptoms and signs for example when there is deranged autonomic dysfunction, or when there is abnormality in the renin angiotensin system. It is an essential book for trainees in cardiology and neurology, and is recommended for any medical library.

Adel Al Jishi (Bahrain)

### Focal Peripheral Neuropathies

#### 3rd Edition

Ed: John D Stewart  
ISBN: 0-7817-1717-5  
No. of pages: 580  
Price: US\$95.00 / £69.00  
Publication Date: 2000  
Publisher: Lippincott, Williams & Wilkins

This is the third Edition of a marvellous publication with descriptive, illustrative and clinically applicable discourse of focal peripheral neuropathies. There are two dozen chapters starting with the structure of the peripheral nervous system including Electron micrographic description. The author has given a good explanation of the pathologic processes producing peripheral neuropathies, what generates electrical activity and how it is derailed in the peripheral neuro lesions – acute to chronic. Diagnostic procedures are described in detail. The author from the 5<sup>th</sup> chapter onwards describes peripheral nerve lesions from upper cervical spinal nerve, cervical plexus and nerves of the neck. There is vivid description of brachial and lumbar-sacral plexuses with illustrative details. The lesions of the individual nerves of upper and lower limbs and pelvis are meticulously given. The flow of the book is excellent and the reader will enjoy going over it. It is perhaps one of the rare books of its kind dealing only with focal neuropathies. The publication is strongly recommended for practising neurologists, neurosurgeons and orthopaedic surgeons interested in dealing with focal peripheral nerve diseases. It is also a must for institutional Libraries.

Editor-in-Chief

### Parkinson's Disease and Movement Disorders

#### Diagnosis and Treatment Guidance

Editors: Charles H Adler and J Eric Ahlskog  
ISBN: 0-896-03607-3  
No. of pages: 474  
Price: \$99.50 (hard cover)  
Publication Date: 2000  
Publisher: The Humana Press

The 35 chapters of this book are written by 35 different authors, each a highly experienced clinician and researcher. The book contains an immense amount of currently available information about various move-

(cont. on p. 16)

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## What's New in Neurology...

### Special Product Highlight

#### World Federation of Neurology - Seminars in Clinical Neurology

##### *Neurologic Bladder, Bowel and Sexual Dysfunction*

Volume Editor: Clare J. Fowler

ISBN 0-444-50678-0

#### Contents:

Editor's Preface

Chapter 1: A neurologist's clinical and investigative approach to patients with bladder, bowel and sexual dysfunction - C.J. Fowler (London, UK)

Chapter 2: Urinary incontinence and retention - C.M. Brady and C.J. Fowler (London, UK)

Chapter 3: Constipation and fecal incontinence - C.M. Brady (London, UK)

Chapter 4: Neurogenic sexual dysfunction in men and women - C.J. Fowler and E.M. Frohman (London, UK and Dallas, TX, USA)

Chapter 5: Multiple sclerosis, other myelopathies and spinal cord injury - E.M. Frohman (Dallas, TX, USA)

Chapter 6: Cauda equina disorders - J.D. Stewart (Montreal, PQ, Canada)

Chapter 7: Peripheral neuropathies - J.D. Stewart (Montreal, PQ, Canada)

Chapter 8: Parkinsonian disorders and pure autonomic failure - R. Sakakibara (Chiba City, Japan)

Chapter 9: Brain diseases - R. Sakakibara and C.J. Fowler (Chiba City, Japan and London, UK)

Text-based multiple choice questions

To view the contents in more detail, go to <http://www.wfneurology.com> and click on "Publications" in the left-hand bar.

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Elsevier Science will have a booth at the meetings listed below. Please visit our booth to browse the latest releases in our book program, see on-line demonstrations of our electronic products and services, and to get free sample copies of our journals.

#### Associated Professional Sleep Societies 15<sup>th</sup> Annual Meeting

5-10 June 2001, Chicago, USA  
Booth number 821

#### XVII World Congress of Neurology

17-22 June 2001, London, UK  
Booth number 3, Earls Court 2

#### XIV International Congress on Parkinson's Disease

28-31 July 2001, Helsinki, Finland  
Booth number B14

We look forward to seeing you!



### World Congress of Neurology

As mentioned in the "Come and Meet us" section above, we will be attending the World Congress of Neurology from 17 to 22 June in London. Please come and visit us on booth number 3 in Earls Court 2. In addition to free sample copies of all our key neurology journals - including Journal of the Neurological Sciences - we will also have free copies of The Lancet, and NewScientist.

In addition to the journals, we will have all our bestselling and most recently published neurology books and book series on display for you to browse at your leisure. Titles on display include volumes from the prestigious Handbook of Clinical Neurology Revised Series, Handbook of Neuropsychology, 2<sup>nd</sup> edition, and Supplements to Clinical Neurophysiology.

In the Electronic Corner you will be able to see our complete package of electronic services, and be able to get hands-on experience yourself as well. Each exhibit day a different service will be demonstrated including the Lancet Neurology Network on Tuesday and Friday ([www.lancetneuronet.com](http://www.lancetneuronet.com)), Neuroscion on Monday and Thursday ([www.neuroscion.com](http://www.neuroscion.com)), and NewScientist's website on Wednesday ([www.newscientist.com](http://www.newscientist.com)).

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### Clinical Neuroscience Research

#### Volume 1/3 out now!

The Official Journal of the Association for Research in Nervous and Mental Disorders

Editor-in-Chief: William E. Bunney, Jr., M.D., Department of Psychiatry, University of California, Irvine, CA, USA.

Volume 1/3 is a special issue entitled "Normal and Pathological Development of the Nervous System", Part I, guest-edited by Dr. Michael I. Posner from the Sackler Institute in New York.

#### Contents:

Normal and pathological development of the nervous system, Pages 173-174  
Michael I. Posner

Neurogenesis in the adult mammalian brain, Pages 175-182  
Nicholas B. Hastings et al

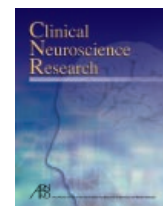
Asymmetry, stem cells and the emergence of function, Pages 183-186  
Ron McKay

From genes to therapies: the role of animal models, Pages 187-193  
Alcino J. Silva et al

Tracking the decline in cerebral glucose metabolism in persons and laboratory animals at genetic risk for Alzheimer's disease, Pages 194-206  
Eric M. Reiman et al

Genes and attention-deficit hyperactivity disorder, Pages 207-216  
James Swanson et al

Williams syndrome: an exploration of neurocognitive and genetic features, Pages 217-229  
Ursula Bellugi et al



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## What's New in Neurology...

Models of temporal processing and language development, Pages 230–237

Albert M. Galaburda et al

Erratum to Physiologic roles for the heme oxygenase products carbon monoxide, bilirubin and iron: links to neuroprotection in stroke and Alzheimer's disease [Clin. Neurosci. Res. 1 (2001) 45–52], Page 238  
David E. Barañano et al

For more details on the Journal, go to: <http://www.elsevier.com/locate/clires>

For more details on the Association, go to: <http://www.arnmd.org>

### Journal of the Neurological Sciences

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(cont. from p. 13)

ment disorders and will help physicians to distinguish between them as well as providing a basic understanding of treatment options needed in active practice. The first half of the book is devoted to the most common disease of Parkinsonism. The second half covers other movement disorders such as tremor, dystonia, chorea, myoclonus, tics, gait disorders, the ataxias, conditions resulting in spasms, restless legs syndrome etc. In a nutshell this book provides comprehensive coverage of Parkinson's disease and other movement disorders. It is most useful for family practitioners, neurologists, gerontologists and residents, and is an appropriate addition to Institutional libraries.

*Editor-in-Chief*

## Merritt's Neurology

### 10th Edition

Editor: Lewis P Rowland  
 ISBN: 0-683-30474-7  
 No. of pages: 1002  
 Price: \$89.00  
 Publication date: 2000  
 Publisher: Lippincott, Williams & Wilkins

This is the famous textbook of neurology dedicated to H. Houston Merritt. It contains contributions from 98 authors and all of them have given masterly accounts of their experiences in managing diseases of the nervous system. The book starts with chapters related to symptoms of neurological disorders, how to select diagnostic tests etc, and then goes on to common neurological problems such as infections of the nervous system, vascular diseases, etc. The last few chapters are related to paroxysmal disorders, systemic diseases and General Medicine, environmental neurology, rehabilitation and ethical and legal guidelines. The majority of chapters are a source of comprehensive knowledge about diseases taking account of technological advances in investigative procedures. The authors deal with molecular genetics and their impact on the diagnosis and management of patients. Extensive changes are in evidence in the 10<sup>th</sup> edition of this one volume textbook of neurology and it is an ideal book for medical students, practising neurologists, general physicians and institutional libraries.

*Editor-in-Chief*

## Child Neurology

### Sixth Edition

Editor: John H Menkes and Harvey B Sarnat

ISBN: 0-7817-2385-X  
 No. of pages: 1280  
 Price: \$115.00  
 Publication Date: 2000  
 Publisher: Lippincott Williams & Wilkins

This is one of the most important books on neurological problems in children. The sixth edition provides updated, comprehensive coverage of child neurology. It is absolutely true that a large number of neurological problems are peculiar to childhood. These include metabolic, hereditary degenerative, chromosomal abnormalities, neuroembryology and storage diseases etc, and all these are discussed succinctly in this book of 16 chapters with contributions from 18 authors. Infections, trauma, tumours and cerebrovascular diseases are also discussed. This book is most useful not only for paediatric neurologists but also for neurologists in many countries of the world who have to handle neurological problems from infancy to old age by themselves. An investment in this book by any institutional library will be rewarding.

*Editor-in-Chief*

## Neurology

### 6th Edition

Editors: Howard L Weiner, Lawrence P Levitt, Alexander Rae-Grant  
 ISBN: 0 683 30497 6  
 No. of pages: 282  
 Price: \$24.95  
 Publication Date: 1999  
 Publisher: Lippincott, Williams & Wilkins

This volume is now in its sixth edition, having first appeared in 1973 which testifies to its popularity. It also indicates the need by House Officers for a handy portable guide to practical neurology. The present edition has been brought up to date but the "problem orientated" approach has been maintained. Thus there are chapters on coma, vertigo-dizziness, dementia, and traumatic brain injury as well as more usual chapters on stroke, multiple sclerosis and epilepsy. This edition has been updated with a section on scanning and I liked the remark when describing the technique of MRI "...pulsating radio waves (heard as clicking sounds by the patient) and magnetic field (which the patient does not feel)". This is a useful book for students and Junior doctors working in a well-equipped hospital in a developed country.

*R Godwin-Austen*  
 London, UK

## CALENDAR

\* = Meeting endorsed by the Continuing Education Committee of the WFN

### 2001

#### XIV International Congress on Parkinson's Disease

28-31 July 2001

Finlandia Hall, Helsinki, Finland  
 Contact: CongCreator CC Ltd, PO Box 762, FIN-00101 Helsinki, Finland  
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 Fax: +358 9 4542 1930  
 E-mail: secretariat@concreator.com  
 URL: <http://www.concreator.com/icpd-2001>

#### 4th Congress of the European Paediatric Neurology Society

13-16 September 2001

Baden-Baden, Germany  
 Contact: AKM Congress Service GmbH, Obere Schanzstraße 18, D-79576 Weil am Rhein, Germany  
 Tel: +49 7621 98330  
 Fax: +49 7621 78714  
 E-mail: [akmweil@akmcongress.com](mailto:akmweil@akmcongress.com)

#### European Charcot Foundation Symposium on The Progressive Phase of MS; its Pathology and Treatment

(including the 7th European Charcot Foundation Lecture by Prof. P. Soelberg Sørensen on The role of IVIG in the Treatment of Secondary Progressive MS)

18-21 October 2001

Venice, Italy  
 Contact: European Charcot Foundation, Heiweg 97, 6533 PA Nijmegen, the Netherlands  
 Tel.: +31-24-3561954  
 Fax: +31-24-3540920  
 E-mail: [info@charcot-ms.org](mailto:info@charcot-ms.org)

## Policy Statement

Although World Neurology is the only medium to go to every neurologist in the world (approximately 22,000 in 84 countries), it is not possible to publicise every neurological meeting that takes place. The prime aim of the Calendar is to notify those meetings that are sponsored by the WFN (World, Continental and Regional Congresses), its Research Groups and Corporate Members of the Research Committee. Notifications of meetings of National Societies are included only if there is significant international contribution. If space allows, others may advertise in the Calendar, in which case a charge of £125 is made. Contact Mr. Keith Newton at the WFN Secretariat, 12 Chandos Street, London W1G 9DR, UK. E-mail: [WFNLondon@aol.com](mailto:WFNLondon@aol.com) for further information.