Infection May Be Culprit in Post-H1N1 Narcolepsy

BY SHARON WORCESTER
Elsevier Global Medical News

The onset of narcolepsy during a 10-year period in China was highly correlated with seasonal and annual patterns of upper airway infections, and was generally independent of H1N1 influenza vaccination, contrary to reports of narcolepsy follow-

ing H1N1 vaccination in northern Europe and other areas. Self-reported data on the month and year of narcolepsy onset in 629 patients who were diagnosed between September 1998 and February 2011 indicate that onset is most frequent in April and least frequent in November in this population, with a nearly sevenfold increase from trough to peak. Dr. Fang Han of Peking University People’s Hospital, Beijing, and colleagues reported.

A greater-than-threefold increase in narcolepsy onset occurred about 6 months following the 2009 H1N1 winter influenza pandemic, but interviews with 142 patients who recalled whether they were vaccinated against H1N1 revealed that vaccination was not likely related to the increase, because only 8 (5.6%) of the patients reported having been vaccinated, the investigators said (Ann. Neurol. 2011;70:410-7).

Furthermore, about 25% of 150 patients recalled having been sick with an infection within a few months of narcolepsy onset, and 85% of those reported symptoms of upper airway infection, including 2 who reported “strep throat.” Animal studies suggest that about 80% of hypocretin/orexin-producing neurons must be lost before symptoms of narcolepsy are exhibited, which could explain the 6-month delay between winter airway infection and narcolepsy onset occurrence, they noted.

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World Congress of Neurology 2011

The program for the 20th World Congress of Neurology in Marrakesh, Morocco, Nov. 12-17, includes a line-up of scientific and teaching sessions — and a host of social events with a decidedly local flavor.

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A Novel Approach To Research

We all want to bring the best medical care to our patients, and it is pretty clear that diagnostic methods and therapies are constantly improving. Even though it is difficult for the practitioner to keep up to date, I think we can all agree that this is a good thing. There are many aspects of medical research, some certainly seem exotic and far removed from anything useful, but we need a variety of types of research if we are to continue moving ahead.

My favorite example recently is the rapid development in assessing a person’s genome. Currently, if a genetic disorder is suspected, typically the specific mutation is evaluated. An alternative, available even to the public, is an array of several thousand SNPs (single nucleotide polymorphisms). Whole exome analysis is becoming available, and may even be cheaper than assessing several specific mutations. Why not get the whole thing for less? But the whole exome is not really everything — that is the whole genome and even that will be possible in a few years. And, what is possible will eventually move into clinical practice — the question is not “whether,” but “when.”

Much of the early research requires experimental animals, and such research is constantly under attack. A new novel illustrating both the value of animal research and the threats on it, Uncoged, is reviewed by Jasper Daube on page 15 of this issue of WORLD NEUROLOGY. His review piqued my interest, so I read the book as well. It is a short novel with some extremes in the story line and stereotyped characters, but fast-paced and engrossing. Could some of the disasters in the book really happen? Could an antibotic-resistant variant of bubonic plague be an act of terrorism? Not impossible, and maybe this recently almost happened! The book certainly shows how animal research is important.

When you are discussing advances in medicine with your patients, there is value in reminding them about the role and importance of research including animal research.

Dr. Tarakad Ramachandran has been elected President of World Neurology Foundation (WNF), a body that promotes neurological care and education in countries in need and supports the World Federation of Neurology (WFN) and other neurological associations in accomplishing that mission. He has been associated with the Foundation for more than a decade and was Vice-President from 2007 until he succeeded Dr. Michael Finkiel as President in April.

Dr. Ramachandran has a strong interest in vascular neurology (stroke medicine) and is highly regarded nationally and internationally as a clinician and educator. He moved to Syracuse, N.Y., USA, in 1976 from the United Kingdom, where he trained in internal medicine. After 2 years of residency and a year of chief residency in neurology at State University of New York’s Upstate Medical University, Syracuse, he was a fellow in neuromuscular diseases and electrophysiology at Boston University School of Medicine. He returned to Syracuse in 1980 to pursue his career in neurology at Crouse and University hospitals.

In addition to being a full academic professor in neurology, Dr. Ramachandran also has held positions as clinical professor of neurosurgery, internal medicine, and family medicine and a lecturer for the Center of Bioethics and Humanities at Upstate Medical University.

Dr. Ramachandran chaired Crouse’s Operation Stroke Committee from 1996 to 2000. As chief of neurology at Crouse, he was instrumental in creating the hospital’s stroke unit, the first in the upstate New York region to be designated with “Gold Plus” performance achievement from the American Stroke Association. He also was active in establishing the stroke unit at Upstate Medical University, from which he retired in 2010. He is presently director of neurosciences at Crouse Hospital and professor emeritus in neurology and psychiatry at Upstate Medical University.

Dr. Ramachandran has published widely and has received many honors and awards. In 2007, the American Academy awarded him the A.B. Baker Teaching Award; and, in 2008, he was the recipient of the AAN’s Kenneth M. Vite Jr. Patient Advocate of the Year award for helping establish an imaging center in Pune, India, to provide free computerized tomography scans and free clinics to the poor. He used the clinics as a base for teaching Indian medical students and residents. This year, he received the Leonard Tow Humanism in Medicine Award from the Arnold P. Gold Foundation for outstanding compassion in the delivery of care; respect for patients, their families, and health care colleagues; and clinical excellence.

As a delegate of the World Stroke Foundation, he participated in the inauguration of the Regional Asian Stroke Congress and first Indian Stroke Association Meeting, endorsed by the World Stroke Federation, at Chennai, India, in 2006. Ever since, he has been a visiting faculty at the Indian Stroke Association’s annual meetings and has contributed significantly to neurological training and teaching elsewhere in India.

Dr. Ramachandran is a fellow of the American Academy of Neurology. He also holds master’s degrees in business administration from SUNY Binghamton University and in public health from Upstate and Syracuse universities.
The best time to plan change is during stability, which is also the most challenging time to do it. The World Federation of Neurology has grown from strength to strength in its half century of existence, but neurology and the world have been changing even more rapidly, and it takes careful and continual planning for us to keep pace with them.

Our administration began with a planning and priorities retreat in London in July 2010, where we reformulated the WFN mission to foster quality neurology care and brain health worldwide. Quality implies standards. One way to set standards is by evaluating what we endorse, so the WFN has formed a Standards and Evaluation Task Force made up of Sarosh Katrak (India) and Charles Warlow (UK), and chaired by Aksel Sva (Turkey), which reviews applications to use the WFN logo for the endorsement of congresses and meetings. Our activities are guided by the answer to four questions:

► What is the value? We favor low-cost, high-impact activities.
► What is the synergy? How can the activity be leveraged within the WFN or with other organizations?
► What is the viability? Can we afford to disperse our limited resources on one-off projects? We need to know the activity will either be completed with the allocated resources or that another organization or government will carry on with the project.
► What will be the process of evaluation? What gets measured, gets done.

In the first phase of this administration, we have kept the committees small so that members could learn to work with each other and with the mission and guiding questions in mind. We have set our priorities, and for the first time have begun a grant review process and funding of member-initiated projects, with several being cofinanced by other organizations, such as the World Stroke Organization and the International League Against Epilepsy. The Grants Review Committee is chaired by me and includes Murat Emre (Turkey), Sarosh Katrak (India), and Jun Kimura (Japan and USA).

All appointments within the WFN have been made for 2 years (tenures of positions ending on Dec. 31, 2011). Now that priorities are set and a number of projects have been funded, opportunities for new appointments and enlargement of the number of task forces will allow for wider participation by members of the WFN.

The World Congress of Neurology (WCN) in Marrakesh, Morocco, Nov. 12-17, will be a great platform for our members to interact, and by all indications it is going to be a landmark event. Registrations to date are comparable with the period leading up to the 2009 Congress in Bangkok, with a total of more than 1,400. The scientific program is outstanding because of the combined efforts of the numerous WFN committees and their colleagues on the Moroccan local organizing committee, who have involved the entire region in the planning. The king of Morocco, His Majesty Mohammed VI, will be sponsoring a gala dinner. This is the first time that a head of state has done so for a World Congress of Neurology, and we are honored and grateful. In addition to the Council of Delegates and the meetings of the various committees and task forces, WFN Vice-President Werner Hacke and Donna Bergar, chair of the Applied Research Committee, will convene a special session of the Applied Research Committee and brain specialty, neurology subspecialty, and related organizations to integrate and collaborate the activities of the diverse organizations dealing with the brain. This is to complement the World Brain Alliance (World Neurology, April 2011, p. 3; June 2001, p. 3). Finally, the updated and enhanced WFN website will be launched at the Marrakesh Congress by Dr. Jerome (Pete) Engel, the web editor and his committee members.

The first phase of our administration has set the stage for an accelerated second phase: Festina lente (make haste slowly). I am looking forward to seeing you in Marrakesh!

WCN 2011

Countdown to Marrakesh

The program for the 20th World Congress of Neurology in Marrakesh, Morocco, Nov. 12-17, includes a line-up of scientific and teaching sessions – and a host of social events with a decidedly local flavor.

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n keeping with this year’s theme of “With Africa, for Africa,” the scientific program for the 20th World Congress of Neurology will include several sessions that focus on the practice of neurology on the continent, in addition to presentations on the latest research findings and new therapies.

Beginning on Saturday, Nov. 12, there will be a teaching session on neurological disorders in sub-Saharan Africa. Other topics during the course of the congress include neuroepidemiological issues in Africa, the history of neuroscience in the Maghreb, and neurological care policy in Africa. There will also be three sessions covering dementia, epilepsy, and cognitive impairment in developing countries.

In all, there will be 13 plenary lectures given on an array of neurological topics by leading experts. Among those featured speakers are:

► Prof. Christian E. Elger, who will deliver the Soriano Lecture on Sunday, Nov. 13, titled “Key Questions on Epileptology.” Prof. Elger is the director and head of the department of epileptology at the University of Bonn, Germany. He has held research fellow posts at the University of Zurich, Switzerland, and the University of Tennessee, in Knoxville, USA. He has served as president of the German Society of Clinical Neurophysiology and chairman of the German division of the International League Against Epilepsy, where he has been a member of the Committee of European Affairs. Prof. Elger is an associate editor for Epilepsy & Behavior and has published numerous articles on experimental and clinical epileptology, and cognitive research.
► Dr. David Zee, who will lecture on “Vertigo and Balance” on Tuesday, Nov. 15. Dr. Zee has been a member of the medical community at Johns Hopkins University in Baltimore, Md., USA, for more than 4 decades as a student and faculty member. He has a special interest in vision and eye movements, cerebellar function and motor learning, and vestibular disorders. He has received the Ottorino Rossi Award from the University of Pavia in Italy for his work on eye movements, and the Hallspe-Nylen Medal of the Hårány Society in Sweden. He served as the inaugural Visiting Professor of Neurological Education at the Mayo Clinic in Rochester, Minn., USA.
► Prof. Stephen Davis, who will lecture on “Translational Stroke Research” on Thursday, Nov. 17. He is the inaugural Professor of Translational Neuroscience at the University of Melbourne, Australia, and is based at the Royal Melbourne Hospital, where he is the director of neurosciences and continuing care, director of neurology and director of the Melbourne Brain Centre at the hospital. Prof. Davis is the immediate past-president of the Australian and New Zealand Association of Neurologists and a past-president of the Stroke Society of Australasia. He is currently on the boards of several journals related to neurology and stroke and is the recipient of numerous distinguished awards on the translational stroke research.

Social Events

WCN 2011 participants will be treated to especially unique and enchanting social events. On Sunday, Nov. 13, there will be a Moroccan-themed opening ceremony, followed by a welcome reception at the congress venue.

The highlight of the social events program will be a gala dinner on Tuesday, Nov. 15, sponsored by the king of Morocco, His Majesty Mohammed VI. The dinner will be held at the renowned restaurant, Chez Ali, where the five-course feast will be served in an authentic Moroccan setting with caidal tents. During the meal, there will be an unforgettable performance of traditional music and dance by Moroccan performers. Chez Ali is considered to be one of the city’s top restaurants in the city.

The Congress at Your Fingertips

► For more information on WCN 2011, go to www.wcn-neurology.org
► To access the interactive scientific program online, go to www.sessionplan.com/WCN2011
► Delegates from Africa and developing countries on other continents are eligible for significant discounts on registration. For more information, go to www2.kenes.com/wcn/RegAcc/Pages/Reg.htm
Care, Research, and Education Are Society’s Focus

Burkina Faso is a small, landlocked country in West Africa bordering on the Ivory Coast, Mali, Ghana, Togo, Benin, and Niger. Of its total population of 14 million, 52% are female, about 48% are younger than 15 years of age, and 78% live in rural areas. The country is fairly stable politically and as a society, but its gross economic and development data are those of a low-income country. It has three schools of medicine, one of which is private.

Health Issues, Clinical Practices
There are fewer than 1,000 physicians in Burkina Faso, so the country has not yet met the World Health Organization’s criteria of 1 physician per 10,000 inhabitants. Its health policy is based on the principles laid out in the Declaration of Alma Ata (WHO, 1978) and the Bamako Initiative (WHO, UNICEF, 1987).

Infectious diseases, mainly in children, are the priority of health policy makers, although HIV/AIDS infection (which affects about 2% of the population, many of whom are adult) presents a significant neurological disease burden. Nontransmissible diseases such as high blood pressure, stroke, diabetes mellitus, and nutritional disorders are increasing and of concern to doctors and policy makers. Health facilities are concentrated in the urban areas of Ouagadougou and Bobo Dioulasso, which are where almost all of the country’s 2,000 hospital beds are to be found. The country obtained the first of three CT scanners in 2000, and its first EEG machine in 1992. MRI is not available in Burkina Faso.

BY JEAN KABORE, MD
Dr. Kabore is president of the Burkina Faso Society of Neurology and chair of the neurology department of Yalgado Ouédraogo (university teaching hospital) in Ouagadougou, Burkina Faso, where he also practices as a neurologist.

Health insurance and third-party payers are uncommon, leading to poor clinical practice and a high incidence of herbal and traditional medicine practices.

Cardiovascular Disease Deaths Spike in Poor Countries
A global analysis released ahead of last month’s United Nations meeting in New York on noncommunicable diseases, revealed that some of the poorest countries in the world have among the highest age-standardized mortality rates of cardiovascular disease (CVD), according to a statement from the World Stroke Organization (WSO).

“It is no longer the case that the majority of deaths are caused by infectious disease,” Prof. Bo Norrving, president of the WSO, said in the statement. “This data provides the evidence for the necessity of [the] summit; the world needs to invest much more and much more quickly in preventing and treating CVD. There is no time to lose.”

The organization said that the data in the Global Atlas on Cardiovascular Disease Prevention and Control, a joint publication of the World Health Organization (WHO), the World Heart Federation, and WSO, highlight the increasing discrepancies in the number of cases and deaths of CVD between high- and low-income countries.

The percentage of premature deaths from CVD in low-income countries was reported as more than double that in high-income countries. Other data in the publication indicated that efforts driven by government policy and at the individual level to curb CVD risk can substantially reduce the health and socioeconomic burden caused by CVDs.

“Heart disease and stroke, together with other cardiovascular diseases, are often wrongly seen as diseases of affluence, although they affect the poor as well as the rich,” said Dr. Shamil Mirza, the WHO’s coordinator of CVD, in the statement. “Although death rates from CVD have been declining in high-income countries over the past 2 decades, they have increased at an astonishingly fast rate in low- and middle-income countries. Now is the time for us to invest in affordable health interventions to ensure that the world’s poorest people are not subject to the growing CVD burden in addition to communicable diseases.”

CVD is the biggest cause of deaths worldwide, even though it could be prevented through lifestyle modifications such as reducing tobacco use and alcohol consumption, eating healthily, exercising regularly, and improving primary care. In 2008, there were more than 17 million CVD deaths worldwide, with 82% of those deaths occurring in low-income and middle-income countries and 3 million occurring before the age of 60.

Prof. Pekka Puska of the World Heart Federation said that governments could play an important role in reducing exposure to CVD by introducing policies that ban tobacco, limit the sugar, saturated fat, and salt content of foods, encourage physical activity, and raise taxes on alcohol. He emphasized that such steps to reduce the risk factors for CVD together with improved access to primary health care could save millions of lives.

Each Oct. 29, the World Stroke Organization (WSO) and its members around the world mark World Stroke Day to promote global awareness of the incidence and consequences of stroke and CVD and advance its campaign to reduce unnecessary deaths from this preventable disease and provide access to care for its victims.

In 2010, the WSO launched the “in 6” advocacy campaign—a reference to the fact that one in six people worldwide will have a stroke in their lifetime and every 6 seconds someone will die from a stroke. In addition to promoting awareness of stroke and its prevention, the WSO also fosters best clinical practices and facilitates research and teaching in the field.
**Gustavo Román**

**Román Elections** • from page 1

President of the World Federation of Neurology and his coauthors (Arch. Neurol. 1987;44:21-3). After specializing in neurology in 1983, I completed a neurology residency at the University of Vermont in Burlington, USA, under the direction of the late Charles M. Poser, and a fellowship in neuroepidemiology directed by Prof. Daniel Perl.

**Investigations in Tropical Neurology**

On my return to Colombia, my interests turned to tropical neurology, and I coauthored one of the first books in Latin America on tropical neurology (Toro G, Navarro-Román LI, Román GC. Tropical Neurology: Neurorheological Aspects of Tropical Medicine. Colombiana: Bogotá, Colombia, 1983). The year before that, I had met Dr. Bruce Schoenberg, then chief of the neuroepidemiology branch at the National Institutes of Health (NIH) in Bethesda, Md., USA, and Dr. Peter Spencer, a neurologist at the Albert Einstein College of Medicine in New York, who were in Bogotá to investigate an outbreak of tropical spastic paraparesis (TSP) in Colombia. During the next 2 years, the National Institute of Health of Colombia sponsored an intensive research study on TSP and dysarthria and I worked in the small island of Turbo on what would become my baptism of fire introduction to the neuroepidemiology. Under Dr. Schoenberg’s masterful direction, we were able to describe the natural history of this geographic focus of TSP (Ann. Neurol. 1985;17:361-5; Neurology 1985;35:118-70). Soon after that, I joined the neurology faculty at Texas Tech University in Lubbock, USA, and within a short while, I resumed working with Dr. Schoenberg and Dr. Peter Spencer on another outbreak of TSP, this time in the Seychelles Islands. We eventually confirmed the disease’s retroviral origin, and the history of the discovery of HTLV-1 myelopathy may be recently reviewed (Lancet Neurol. 2007;6:104-5).

In 1990, I succeeded Dr. Schoenberg, who had become seriously ill, as chief of neuroepidemiology at the NIH. I continued the research on TSP in the Caribbean and South America and among other topics, organized a workshop that proposed the research criteria for vascular dementia, which are currently used worldwide (Neurology 1993;43:250-60). One of the most challenging research activities at the NIH was when we participated in a study of an epidemic of optic and peripheral neuropathy in Cuba that had affected more than 50,000 people and was probably the largest neurological epidemic of the past century.

**Same Principles, Different Diseases**

During this time, I was quite active with the WFN research groups on neuroepidemiology and tropical neurology. We conducted numerous courses on neuroepidemiology that were later published as a research network that continues to provide data on the epidemiology of dementia, Alzheimer’s and Parkinson’s diseases, and vascular dementia in China, Spain, Argentina, and Mexico.

In 2000, I joined the University of Texas Health Science Center at San Antonio, USA, where I established the Alzheimer Disease Memory Clinic, which was invited to join the Alzheimer Research Consortium. I participated in a large study funded by the NIH on prevention of lacunar strokes and cognitive loss with control of hypertension.

Last year, I was selected as the Jack S. Blanton Distinguished Endowed Chair and director of the Alzheimer’s Disease Clinical and Research Center at the Methodist Neurological Institute in Houston, USA. In this capacity, I continue to apply the principles of epidemiology and the teachings of my mentors in clinical neurology and neuropsychiatry to find a cure to the cruelest neurological epidemic of our time, Alzheimer’s disease.

I began serving as Elected Trustee of the WFN in 2009 during the World Congress of Neurology (WCN) in Thailand, and at the request of the President of the WFN, I accepted the task of directing the WFN Latin American initiative. As Elected Trustee, I have participated in all the main administrative decisions of the current board of directors of the WFN. Also, I served as faculty in the teaching course for African neurologists organized in 2010 by the European Federation of Neurological Societies (EFNS) and the University of Cobicodi, in Abidjan, Ivory Coast, and I was instrumental in inviting and welcoming Ivorian neurologists as new members of the WFN. I lectured at the meeting of the Pan American Society of Neuroepidemiology in Punta del Este (Uruguay) and the 3rd Latin American Meeting of the Dementia Group of the WFN in Buenos Aires (Argentina). I was invited to serve as adviser for the scientific program of the forthcoming 20th World Congress of Neurology in Marrakesh, Morocco, and of the 13th Pan American Congress of Neurology (4-8 March, 2012) in La Paz, Bolivia.

**Mission Statement**

Very early in life I learned that education is critical to overcome the limitations imposed by environment and economic restrictions. I believe that education is also the answer to many of the problems resulting from uncontrolled risk factors in health and disease such as poverty, malnutrition, trauma, and violence, among others, that are the prevalent causes of many neurological diseases; whereby, public health practice and policy becomes an important tool for neurologists. By the same token, increasing the number and the educational level of neurologists must result in tangible benefits for the countries and their peoples. With the change to a biennial mode of the World Congress of Neurology, the duration of service of the Elected Trustees has also been limited to only 2 years. Therefore, I am seeking re-election as Trustee of the WFN in order to bring to full fruition the projects I have already started.

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**John Wolke**

**Wolke Elections** • from page 1

introduced me to the fascinating field of specialized light and electron microscopy. Prof. Jemnekens and I subsequently collaborated with him and Prof. John Newsom-Davis and Prof. Hans Oosterhuis in research on congenital myasthenic syndromes.

In 1988, I defended my doctoral thesis on human motor end plates, in which I showed that nerves continue to create new end plates during aging and disease. This notion of plasticity of the end plates is very reassuring. I argued that the skeletal muscle satellite cells around human motor end plates may facilitate this regenerating process. The year before I defended my thesis, I was one of the first researchers to describe the CNS manifestations of Lyme disease (Neurology 1987;37:1031-34).

**Probing the ALS Puzzle**

My colleagues in the department of neurology at Utrech and I lead a research group, focusing our work on multifocal motor neuropathy (MMN), chronic inflammatory demyelinating polyneuropathy (CIDP), and motor neuron disease and amyotrophic lateral sclerosis (ALS). Initially, we described the natural disease course, neurophysiological characteristics, and effects of the treatments for MMN and CIDP. In 2010, we monitored the response of 88 MMN patients to IV immunoglobulin (IVIG) treatment and reported findings that suggested that early IVIG treatment might postpone axonal degeneration and permanent deficits (Neurology 2010;75:818-25). I have compiled a nationwide database of ALS patients with the present research group leader, Prof. Leonard van den Berg, a leading expert of whole genome analysis of ALS. Our goal is to unravel the genetic and environmental factors that could be risk factors or disease-modifying factors for ALS. We believe that this knowledge could inform the development of new treatments. I was very fortunate to collaborate for many years with the eminent stroke neurologist Prof. Jan van Gijn, a former head of the department of neurology at Utrech and one of the founding members of the European Neurological Society. We focused the department’s research on stroke and neuromuscular diseases.

**Education, Research, and Care**

I chaired the department of neurology from 2001 to 2011. My colleagues and I have always tried to bring in enthusiasts, talented students to work with us in our research. Many of these research students will become neurology residents and clinical researchers. Over the years, I have supervised 24 doctoral students, and many of them are now continuing with research or are involved in neurology education. For me, teaching and research go hand in hand. Young doctors should question everything they learn and continue to expand the knowledge base. If they do not do that, who will? I firmly believe that university departments must try to make a difference and improve the scientific basis for good patient care.

At present, all 36 residents of the department combine neurology training with clinical research into ALS, stroke, or epilepsy in children for their doctoral theses. Five of our residents have been appointed professors at other institutions. I have long been involved in the European neurological community, and I see my involvement there as a stepping stone to the global community. Connection and collaboration between neurologists and researchers across the world are important for the development of our specialty. Studies of phenotypes, clinical trials, and genetics improve with the contributions from doctors from various countries because the external validity of results will increase. Of course, the best methodology is a prerequisite.

In 1996, I organized the sixth meeting of the European Neurological Society (ENS) in The Hague. In 2000, Prof. Pamela Shaw, Prof. Nigel Leigh, Prof. Vincent Meiners and the European ALS Study Group to encourage young scientists to pursue ALS research. The group holds low-key meetings at which junior researchers present their work and senior experts and researchers from some of Europe’s leading ALS research centers offer comment and feedback. Such meetings help build mutual trust and foster scientific exchange and the formation of networks. From 2006 to 2009, I chaired the Dutch Society of Neurology. During my tenure as chair, we drew up a new strategy for the emphasis that emphasized quality of neurol ological care, education, scientific developments, and neurological practice. I am currently chairman-elect of the education committee of the Dutch Society of Neurology.

**Mission Statement**

Throughout my career, I have always stressed the equal importance of education and research. In 1988, I received the young investigator prize from the Amsterdam Neurological Society, and in 2001 I received the Winkler award for research on neuropathies and ALS from the Dutch Society of Neurology. The Winkler is awarded every 5 years. In 2010, I received the Vaandragersprijs teaching prize from the society of Dutch neurological residents.

In the next phase of my career, I intend to focus on improving neurology education and quality of neurological patient care. As a WFN Trustee, I would hope to contribute to help setting international standards for neurological education and to improve exchanges between various countries. Second, with the rapid development of research and of special fields of interest in neurology, the specialty as a whole is in need of support and guidance. Training in good clinical thinking can help to achieve just that. Formulation of international accepted standards, guidelines, and practical parameters is an absolute necessity. In both areas, a role for the WFN is evident.
SSRIs May Up Kids’ Risk of Limb Movements in Sleep

BY SHARON WORCESTER
Elsevier Global Medical News

Children who are treated with selective serotonin reuptake inhibitors have fivefold greater odds of experiencing periodic limb movements of sleep than do those who are not treated with SSRIs, according to findings from a retrospective review of polysomnography data.

Nearly a third (31.7%) of 41 children receiving SSRIs at the time of the study experienced periodic limb movements of sleep, compared with only 7.8% of 982 children not receiving SSRIs (odds ratio, 5.45), Dr. Martina Vendrame of Boston University and her colleagues reported.

Furthermore, the median periodic limb movement index in those receiving SSRIs was significantly higher than the index in those not receiving SSRIs (11.2 vs. 6.5), the investigators said (Pediatr. Neurol. 2011;45:175-7).

Although periodic limb movements of sleep have been reported in adults taking serotonergic antidepressants—with one study showing that 44% of adults receiving fluoxetine experienced the symptoms, and others showing that restless legs syndrome (RLS) is exacerbated in up to 10% of adult patients on SSRIs—the current study is one of few that provide information about periodic limb movements of sleep in children and adolescents.

Study subjects were all children who underwent overnight diagnostic polysomnography between January 2009 and April 2010 at a single center. The studies were conducted for various sleep disturbances such as snoring, pauses in breathing, daytime sleepiness, and gasping or snoring in sleep; none was conducted for reports of RLS or periodic limb movements of sleep.

The patients who received SSRIs included 31 girls and 10 boys who had a median age of 15.4 years. The SSRIs were prescribed for depression and included citalopram or escitalopram in 15 patients, fluoxetine in 14 patients, and sertraline in 12 patients.

“The mechanism by which SSRIs may cause periodic limb movements of sleep is not clear, but serotonin-mediated dopaminergic inhibition may represent the underlying mechanism,” the investigators noted.

Although no significant differences in mean periodic limb movements of sleep indices were seen between different SSRIs in this study, it is possible that different doses and timing of administration could result in better control of limb movements, they said, adding that when periodic limb movements of sleep are found, a careful history should be taken to assess whether they are causing sleep disturbance, and also to determine if the child is experiencing RLS.

“If necessary, the use of antidepressants not associated with periodic limb movements of sleep should be considered,” they wrote.
The reflex hammer is surely the universal emblem of the neurologist, and the tendon reflex one of the most important components of the neurological examination.

There is documentary proof that the American neurologist S. Weir Mitchell (1840-1921) had described the response of muscles to the tap of a percussion hammer as early as 1859 and that many physicians were aware of the phenomenon, but the first systematic studies of the knee reflex were described in 1875 by the Germans Wilhelm Erb (1840-1921) and Carl Westphal (1833-1921). In two independent publications, Westphal described the “knee phenomenon,” and Erb, the “patellar-tendon reflex” (Neurology 1989;39:1542-9).

In 1841, the German physician Max Wintrich (1812-1882) introduced the first fashionable percussion hammer to Europe. He introduced a disc (a plethist, a triangular, rubber-headed hammer) (Figure 2). Taylor exhibited his “Queen Square” hammer to the Medical Society of London, the Verner hammer even more so. The famous Queen Square hammer resembled all manner of fashionable percussion hammers, the edge of a large electrode, the foot of a laboratory stand, a table lamp, or similar devices, designed to elicit tendon reflexes. One such hammer, designed in 1901 by Ernst Troemmer (1868-1930) of Hamburg, Germany, became very popular. According to Troemmer, his hammer had the added advantage that the smooth handle of the hammer could easily be cleaned and in a pinch used as a tongue blade!

Another German neurologist, Dr. Bernhard Berliner, who considered it “not very elegant to percuss the knee or Achilles tendon with a paperweight, the edge of a large electrode, the foot of a laboratory stand, a table lamp, or similar devices,” designed a hatchet-shaped hammer (Figure 2), which he said allowed, in most instances, for the elicitation of an existing Achilles reflex through the patient’s boots.

In the United States, Dr. John Madison Taylor (1855-1931) is credited with the design of the first “neurological hammer” (Figure 2). Taylor exhibited his now famous triangular, rubber-headed hammer in 1888, while he was working as a personal assistant to the prominent neurologist, S. Weir Mitchell (1829-1914). The hammer would later be incorporated into the official logo of the American Academy of Neurology.

The Bruce S. Schoenberg International Award in Neuroepidemiology

The Bruce S. Schoenberg International Award in Neuroepidemiology pays tribute to Dr. Schoenberg’s career in training neurologists internationally in epidemiologic methods and validates a promising young investigator from a developing country or Eastern Europe. Dr. Schoenberg was chief of the neuroepidemiology branch at the National Institute of Neurological and Communicative Disorders and Stroke in Bethesda, Md., USA, 1984-1987. The recipient will be recognized at the 64th American Academy of Neurology Annual Meeting in New Orleans, Louisiana, USA, April 21-28, 2012.

Presentation
The recipient is expected to give a 20-minute presentation based on the selected abstract during a scientific session at the 64th Annual Meeting.

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Immunoadsorption May Have Relieved Neuro Symptoms of E. coli

Researchers posit that the therapy may have removed the toxin and activating immune complexes.

BY JENNIE SMITH
Elsevier Global Medical News

A group of people who developed severe neurological symptoms following Escherichia coli infection recovered after being treated with immunoadsorption, a process that removes immunoglobulin G from blood plasma, according to a small observational study in Germany. Whether they would have recovered anyway is not clear.

The evidence for the interpretation that immunoadsorption has caused these people to improve is really weak.

DR. STINGLEE

The Shiga toxin—producing E. coli O104:H4 outbreak, which began in May 2011 in northern Germany, caused enteritis in nearly 4000 Germans and hemolytic uremic syndrome (HUS) in more than 800 by the end of July (WORLD NEUROLOGY, August 2011, p. 1). A number of patients with both enteritis and HUS went on to develop severe neurological complications, including seizures, a week after their enteritis had subsided. The seriousness and diversity of the neurological symptoms accompanying E. coli O104:H4 HUS took many experienced clinicians by surprise, and the symptoms included stimulus-sensitive myoclonus (a type of spasm), psychosis or delirium, severe seizures, and aphasia.

The timing of the onset of neurological symptoms led researchers Dr. Andreas Greinacher and Dr. Sigrun Friesecke of Ernst Moritz Arndt University of Greifswald (Germany) to suspect that an antibody-mediated mechanism was involved. The 12 patients and colleagues’ study were all infected with E. coli O104:H4 and had developed HUS followed by a variety of neurological symptoms (most had more than one).

All but one were female, and all but two had been treated first with therapeutic plasma exchange or complement-blocking antibody (eculizumab) and had not responded. Nine were on mechanical ventilation because of breathing difficulties caused by their neurological symptoms (Lancet 2011 Sept. 5 [doi:10.1016/S0140-6736(11)61253-1]). Patients were treated with IgG immunoadsorption processing of 12 L of plasma on 2 consecutive days, followed by IgG replacement (0.5 g/kg intravenous IgG) as rescue therapy. Eight patients received at least one additional 12-L session of immunoadsorption therapy, and patients whose symptoms returned following therapy received more. Dr. Greinacher and colleagues assessed neurological changes before and after immunoadsorption, using an established scoring system.

The researchers found that in their cohort, composite neurological symptom scores significantly increased in the 3 days before immunoadsorption to 3.0 and improved to 1.0 in 3 days after immunoadsorption. Five patients who were intubated were weaned within 5 days of therapy, two within 4 days, and two patients needed continued ventilation for respiratory problems. All patients survived, and 10 had complete neurological and renal function recovery.

The findings led Dr. Greinacher and colleagues to conclude that their experience showed immunoadsorption “can strikingly improve neurological complications in patients with E. coli O104:H4-associated hemolytic uremic syndrome,” and that this was biologically plausible.

“Onset of neurological symptoms 5-12 days after onset of diarrhea is compatible with a secondary IgG immune response,” they wrote, and “selective removal of IgG antibodies by immunoadsorption with immunoglobulin-binding columns resulted in two effects: removal of activating immune complexes and effective removal of the Shiga toxin itself.”

Although Dr. Greinacher and colleagues conceded that their study was limited by its observational design, the “reproducible response to immunoadsorption in all patients, and especially the repeated response in case of neurological relapse, suggests that improvements were a true treatment effect and not related to the natural course of the illness,” they wrote in their analysis.

However, neurologist Dr. Robert Stingle of the University of Kiel (Germany), who also treated patients with HUS and neurological symptoms, was unconvinced.

Dr. Stingle said in an interview that although his group had treated 52 HUS patients, of whom 27 had developed neurological symptoms during the outbreak, immunoadsorption was not a technique they had considered.

The reason, Dr. Stingle said, “is that we did not think the disease was antibody-mediated. Instead, we went after the toxin.”

“It is not really plausible in my opinion that central nervous system disease develops mediated by antibodies [in the case of E. coli O104:H4] because it takes a long time for antibodies to be available in high titers,” Dr. Stingle said.

“These antibodies, to reach the central nervous system, need to cross the blood-brain barrier,” he said.

Moreover, Dr. Stingle said, plasma separation—which his group did attempt, just as Dr. Greinacher and many other treatment teams throughout Germany did during the outbreak—“was seen to produce no stepwise improvement, though it should have had at least some effect if the disease were in fact antibody-mediated.”

All of the patients in Dr. Stingle’s group also fully recovered, including those with the most severe neurological symptoms. “Most were discharged with no neurological symptoms and some with mild symptoms,” he said of the patients he saw personally.

While it’s certainly an interesting finding that they recovered after immunoadsorption,” Dr. Stingle said of Dr. Greinacher and colleagues’ subjects, their recovery was similar to what his own group had seen without it. “The evidence for the interpretation that immunoadsorption has caused these people to improve is really weak.”

Even if there were another E. coli O104:H4 outbreak, Dr. Stingle said, “I would do the same thing that we did. I would not attempt [immunoadsorption].”

Two of Dr. Greinacher’s coauthors, Dr. Stephan B. Felix and Dr. Jan T. Kielstein, disclosed receiving research support and speaker fees from Fresenius Medical Care, which manufacturers the immunoadsorption technology used in the study. None of the other authors disclosed conflicts of interest. Dr. Greinacher and colleagues’ study was funded by the University of Greifswald and Hannover (Germany) Medical School. Dr. Stingle disclosed that he had no financial conflicts of interest related to his comment.

Correction

The affiliation for Maria Stamelou, MD (WORLD NEUROLOGY, June 2011, p. 12), was incorrect. Dr. Stamelou is now at the Sobell Department of Motor Neuroscience and Movement Disorders in the Institute of Neurology at the University College of London, UK, where she is an honorary clinical assistant and research fellow.
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The possibility that narcolepsy could be a rare side effect of H1N1 flu vaccination was first reported by the Swedish and Finnish medical product agencies in August 2010, with a potential link to Pandemrix – a modified H1N1 inactivated vaccine containing the adjuvant AS03 and squalene/alpha-tocopherol.

Last year, within three major world centers of reference for narcolepsy (Montpellier, France; Montreal, Canada; and Stanford ( Calif.) University, USA), we reported an unusual increase in abrupt-onset narcolepsy-cataplexy diagnosed within a few months of H1N1 onset. Cases were reported with a clear temporal link between vaccination and disease onset (mean, 8 weeks), with occasionally an unusual clinical presentation with rapid development and severity of both excessive daytime sleepiness and cataplexy. Findeitings of the World Health Organization indicated a ninefold increased risk of narcolepsy in children and adolescents aged 4-19 years following vaccination with Pandemrix, and findings of the Swedish Medical Products Agency showed that the relative risk of narcolepsy was 6.6 times higher in vaccinated than unvaccinated children and adolescents. In an accompanying commentary, Dr. Stephen L. Hauser and Dr. S. Claiborne Johnston of the University of California, San Francisco, USA, noted that the evidence of a possible association between infection and narcolepsy, and could point to pandemic H1N1 – in addition to streptococcal infection – as a potential environmental trigger – a potential environmental trigger.

They also noted that if specific peptides of pandemic H1N1 are shown to interact with narcolepsy-associated genes, an understanding of the triggers of narcolepsy may begin to emerge, potentially leading to new approaches for prevention and treatment. As for the emerging concerns about adjuvanted vaccine and narcolepsy risk, Dr. Hauser and Dr. Johnston noted that the findings of this study raise the possibility that narcolepsy following infection and vaccination might represent a common immune response to a similar antigenic challenge – a phenomenon seen with ADEM (acute disseminated encephalomyelitis) that can occur following measles vaccination with an adjuvant or after administration of measles vaccine. In the case of ADEM, the risk is far greater with infection than with vaccination. This study was supported by research grants from the National Science Foundation of China, the Sino-German Center for Research Promotion, the Beijing Municipal Science and Technology Commission, and by the Veterans Administration Research Service. One of the authors, reported serving as a consultant and/or providing expert testimony for both the pharmaceuticals Merck, Mead, and the Federal Trade Commission. Dr. Mignot also has been in discussion with GlaxoSmithKline, the maker of Pandemrix, regarding the funding of contractual research. 

Many Migraineurs Report Unmet Medical Needs

Almost half of patients with episodic migraine report having at least one unmet medical need, according to findings in a population-based survey of more than 20,000 people. The findings suggest that despite the expanding armamentarium of acute migraine therapies, patient satisfaction with treatment is at best low to moderate for many, Dawn Buse, Ph.D., director of behavioral medicine at the Montefiore Headache Center, New York, said at the annual meeting of the American Headache Society in Washington, DC, USA.

Dr. Buse and her colleagues identified five domains of possible unmet treatment needs:

- Dissatisfaction with current acute treatment.
- Moderate or severe headache-related disability.
- Excessive use of over-the-counter medications or barbiturates.
- History of cardiovascular events that might preclude triptan therapy.
- History of cardiovascular events that might preclude triptan therapy.

Those with no unmet needs reported a mean of 2 days per month with headache, compared with 3 days per month for the group with one unmet need, and 5 days per month for those with two or more needs. The most common unmet need was headache-related disability of moderate to severe intensity (19%).

-Michele G. Sullivan

To see a video interview with Dr. Buse, scan the QR code or visit www.clinicalneurologynews.com, click on the video icon, and search for “treatment needs unmet in migraine.”

Simple Screen for Medication Overuse Headache

Asking two straightforward questions – “Do you take an attack treatment more than 10 days per month” and “Is this intake on a regular basis?” – can help clinicians quickly screen and identify patients with medication overuse headache.

The traditional approach to diagnosis of medication overuse headache involving the revised International Classification of Headache Disorders (ICHD-II) criteria requires a face-to-face interview that takes considerable clinician time and expertise. Dr. Virginie Doussset told attendees at the International Headache Congress in Berlin, Germany. So she and her colleagues transformed the second edition ICHD-II criteria into four simplified questions for a patient self-administered screening tool. To determine its sensitivity and specificity, they recruited 79 consecutive patients between September 2009 and February 2010 at the Bordeaux (France) Headache Centre at the University of Bordeaux, where Dr. Dousset is director.

Two questions about attack treatment frequency and regular use of medications were combined and had the best sensitivity (95%) and specificity (80%) for identification of medication overuse headache. The question, “Do you have headaches on 15 days or more per week?” had 81% sensitivity and 85% specificity. A fourth question was dropped.

-Damien McNamara

To see a video interview with Dr. Dousset, scan the QR code or visit www.clinicalneurologynews.com, click on the video icon, and search for “diagnosing medication overuse headache.”
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Array of Genetic Mutations in Hereditary Neuropathies

All patients with pathogenic mutations presented with peripheral neuropathy symptoms before age 1.

BY SHARON WORCESTER
Elsevier Global Medical News

Hereditary neuropathies with onset during infancy are characterized by extensive genetic heterogeneity and clinical variability, according to findings from a study of 77 unrelated patients who presented with symptoms of peripheral neuropathy within their first year of life.

The patients in the study underwent systematic mutation screening by means of direct sequencing of the coding regions of 11 genes, as well as screening of the Charcot-Marie-Tooth type IA (CMT1A) duplication on chromosone 17p11.2–12. Mutations were identified in 35 (45%) of the 77 patients, Dr. Jonathan Baets of the University of Antwerp (Belgium) and his colleagues reported.

Five patients carried a de novo heterozygous mutation in MPZ, EGR2, PMP22, or MFN2; 4 isolated patients were heterozygous for mutations in NEFL or MPZ, the CMT1A duplication, or a partial PMP22 duplication; 5 patients had mutations in MPZ and the CMT1A duplication transmitted as a dominant trait; 20 patients inherited recessive mutations in GADAP1, MTMR2, SBF2, FGD4, PRX, or SH3TC2 from their unaffected parents; and 1 isolated patient had a novel heterozygous AR4G400 Pro mutation in MFN2.

In the study, which is the largest, to our knowledge, of patients with CMT1A, the investigators identified mutations in 35 (45%) of 77 patients, 19 of whom had a CMT1A duplication and 16 of whom had a PMP22 exonic duplication.

In addition, the investigators identified mutations in 11 genes identified mutations in 35 (45%) of 77 patients, 19 of whom had a CMT1A duplication and 16 of whom had a PMP22 exonic duplication. The investigators found that mutations in the CMT1A gene were responsible for 78% of the cases, and mutations in dominant genes were responsible for 3% of the cases.

The investigators noted that the major finding of the study was that mutations in the CMT1A gene were responsible for 78% of the cases, and mutations in dominant genes were responsible for 3% of the cases.

In conclusion, research on the genetics of CMT may lead to better understanding of the disease and potentially to the development of new treatments.

In patients with a congenital disease onset, mutations in dominant genes are more likely to be the case; mutations in recessive genes are more probable in those with progressive delay in motor development in the first year of life—especially if parents are consanguineous.

Axonal subtypes are probably restricted to a smaller subset of genes that may be tested preferentially.

Other findings, such as myelin outfoldings on nerve pathology, may help prioritize molecular testing.

Similarly, severe and early scoliosis, although suggestive of a CMT1A or CMT2 mutation, may also be seen in patients who have mutations in other genes, and can be considered a feature that may be found in many types of severe and progressive neuropathy of early childhood.

In conclusion, reaching a correct genetic diagnosis in children with severe early onset hereditary motor and sensory neuropathy remains a major challenge with conventional screening techniques.

A future solution for this diagnostic conundrum may lie in the more systematic diagnostic application of recently developed techniques for massive parallel sequencing, the investigators wrote.
Bioterrorism Threat Raises Ethics of Animal Research

BY MICHELE G. SULLIVAN
Elsevier Global Medical News

Cardiac arrhythmias and conduction abnormalities are not uncommon in multiple sclerosis (MS) patients who undergo high-dose methylprednisolone infusions for an acute disease exacerbation. Smokers and those with higher body mass indices and saphenous nerve control problems were most likely to develop the problems. But all the disturbances were short lived and none required interventions. Dr. Ali Vashgehani-Farahani and his colleagues reported in a study of 52 patients.

Nevertheless, the high incidence of cardiac arrhythmias during and after methylprednisolone infusion warrants close observation of patients after the treatment. The high-risk groups “benefit from cardiac Holter monitoring 12 hours after the steroid pulse therapy to prevent life-threatening adverse events and identification of possible cardiac complications,” the authors wrote (J. Neurol. Sci. 2011;309:75-78).

Dr. Vashgehani-Farahani of the Tehran (Iran) University of Medical Sciences and his colleagues examined adverse cardiac events in the patients who received high-dose methylprednisolone pulse therapy for acute disease exacerbation at a mean age of 35 years. Most (69%) of the patients had relapsing-remitting MS, followed by secondary (21%) and primary (10%) progressive disease. They had had MS for a median of 5.5 years. All received 1 g of intravenous methylprednisolone diluted in 500 ml of 5% dextrose, infused over 2 hours during a 3- to 5-day period. Patients underwent Holter monitoring 4 hours before the infusion, during the treatment, and for 18 hours afterward.

The most commonly observed problem was sinus tachycardia, which occurred in 56% before the infusion, 65% during the treatment, and 54% afterward, all of which were significant increases over the baseline. Sinus bradycardia and atrial tachycardia also increased significantly with treatment. Bradycardia was present in 4% before the infusion, 9% during it, and 42% afterward. Atrial tachycardia occurred in 5% of patients before treatment and 5% during treatment, but increased significantly to 13% after treatment.

Three patients experienced atrial fibrillation after treatment. The first was a 62-year-old man with a body mass index of 34 kg/m² and bladder and bowel dysfunction. The other two patients had normal BMIs, but both had autonomic bladder and bowel dysfunction.

Some patients also experienced conduction abnormalities, including 10% with sinus arrest or sinus exit block. There were statistically significant increases of premature atrial contraction and premature ventricular contraction both during and after steroid infusions, the authors wrote. “Sinus arrhythmia was present in 10% of the recordings before steroid infusion, which increased to 10% after steroid infusion.” All these types of cardiac arrhythmias were seen in the first 12 hours after pulse therapy.

Ventricular tachycardia, sinus arrest, sinus exit block, atrial fibrillation, and sinus bradycardia were significantly associated with smoking; sinus arrest, sinus exit block, and atrial fibrillation were significantly associated with a BMI of 25 or higher.

Patients with saphenous nerve disturbance were more likely to experience sinus bradycardia and atrial fibrillation. Biventricular dysfunction was significantly associated with sinus bradycardia, sinus tachycardia, atrial fibrillation, and premature atrial contractions.

“Corticosteroids, by their mineralocorticoid activity, result in the retention of sodium and intracellular fluids, causing high blood pressure and congestive heart failure,” and increasing the risk for atrial fibrillation. No financial disclosure information was available in the report.

When I was a junior attending neurologist, I had a multiple sclerosis (MS) patient who was having a relapse. I admitted her to hospital to treat her with intravenous methylprednisolone (IVMP). I had no special concerns about this, since I had treated many MS patients with IVMP with no adverse events at all or only some minor euphoria, or mild dyspepsia. Thus, I was quite inexperienced for the nurse’s call later that day, when she told me that the patient was bradycardic, diaphoretic, and somewhat nauseated. This sounded like a medication side effect but I had given her no such drugs. A consultant cardiologist suggested that the IVMP had a vagotonic effect. She did well, though in a monitored setting. Subsequent courses of IVMP caused significant palpitations and pulse reproduced all of these cardiac abnormalities.

Ventricular tachycardia occurred even after sodium and dextrose infusion. She required a pacemaker, when the bradycardia occurred even after sodium. I recall very clearly because of the unique prominence of her symptoms, which included not only arrhythmia, but also other autonomic findings.

The paper by Vashgehani-Farahani et al. suggests that the IVMP had a vagotonic effect. She did well, though in a monitored setting. Subsequent courses of IVMP caused significant palpitations and pulse reproduced all of these cardiac abnormalities.

The high prevalence of autonomic abnormalities especially of bladder and bowel function are compatible with the latter. The authors’ suggestion of the effect of sodium and fluid balance abnormalities are probably compatible with the latter. The authors’ suggestion of the effect of sodium and fluid balance abnormalities are probably compatible with this.

It would be interesting to make the same observations in other groups of patients who are treated with high-dose IVMP for diseases that are not known to involve the autonomic nervous system. Potential groups may include cancer and transplant patients. The results will teach us much about the effects various diseases and medications have on autonomic function.

What happened to my patient? Over the years, she developed several autonomic issues, including diaphoresis, nausea, and postural hypotension. Ironically these responded partially to IVMP. In her, it is most likely that the MS caused the autonomic abnormalities, beginning with bradycardia, and the IVMP unmasked it.

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

BOOK REVIEW

Bioterrorism Threat Raises Ethics of Animal Research

Uncaged
By Paul McKellips
Vantage Press, 2011

This remarkable book tells an important story from a different perspective. Physicians are well aware of the importance of animal research for the steady improvements in medical care, but many of the public are not. Two recent books, one by P. Michael Conn and James V. Parker titled The Animal Research War, and another by Alistair Morrison, in An Odyssey With Animals, detail attempts by “animal rightsists” to stop animal research, but neither book has attracted public interest in the issue. In Uncaged, Paul McKellips presents the same issues in a riveting thriller that will likely have broader appeal.

McKellips is executive vice president for the Washington, D.C. (USA)-based Foundation for Biomedical Research and an accomplished film and television producer. In this, his first novel, he presents the horror of animal rights’ goals and the serious damage and risk to others that accompany their efforts. A military doctor, Commander “Camp” Campbell, and Lieutenant Colonel Leslie Raines, a medical scientist and expert in infectious diseases, combine their skills to subdue the disastrous results of a presidential ban on animal testing. The ban, which has been instigated by an animal rightsist group, halts all medical research in the country just as a terrorist group unleashes a bubonic plague by releasing infected rats into the United States from ships docking at American ports. The book is a fast-moving thriller in which the two heroes overcome innumerable obstacles in identifying and overcoming the bioterrorist threat to the human race and grapple with ethical issues that arise with animal research.

While the book is a work of fiction, it is based on the death of 40 al-Qaeda insurgents in North Africa who had been working with the plague, possibly to use it as a weapon. The book is dedicated to the “biomedical researchers, scientists, and physicians who work in universities, medical schools, and veterinary schools as well as pharmaceutical companies, government agencies, and the military who are fighting for our health.”
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