

# HIGHLIGHTS FROM INTERNATIONAL NEUROSCIENCE MEETINGS

## *19th World Congress of Neurology Bangkok, October 24th - 30th 2009*

*Brahim M. Tabarki, MD.*

Division of Pediatric Neurology, Department of Pediatrics, Riyadh Military Hospital, Kingdom of Saudi Arabia

The 2009 19th World Congress of Neurology was held in Bangkok, Thailand, from 24th to 30th October 2009. The scientific presentations numbered over 1245, of which 544 were from the platform and over 701 were posters. This meeting provides an overview of recent advances in the diagnosis and treatment of various neurological disorders. We selected 2 plenary sessions of particular interest, to summarize.

### *Plenary sessions*

#### *Neurodegenerative diseases: new strategies in research and therapy. Gene vaccination for Alzheimer's disease.* R. N. Rosenberg

Alzheimer's disease (AD) pathogenesis has been associated with the accumulation, aggregation, and deposition of amyloid beta ( $A\beta$ ) peptides in the brain. Abeta42 immunotherapy provides great potential to treat or prevent AD. A clinical trial with Abeta42 peptide vaccination in AD patients caused meningoencephalitis in 6% of the participants, which was likely due to a Th1 immune response, and was stopped. The study compared in detail the immune response in wild-type mice after vaccination with  $A\beta$ 42 trimer DNA delivered by gene gun and the intraperitoneal injection of  $A\beta$ 42 peptide in combination with the adjuvant QuilA. Antibody titers, epitope mapping, and isotype profiles of the  $A\beta$ 42 specific antibodies were followed through the immunization procedure. Results were as follows: 1)  $A\beta$ 42 trimer DNA vaccination using the Gal4/UAS expression system resulted in high  $A\beta$ 42 specific antibody titers. 2) Epitope mapping showed that both antigens, DNA and peptide, elicited a response towards the known B cell epitope,  $A\beta$ 1-15. 3) The isotype profile of the antibodies differed markedly, a predominant IgG1 antibody response was found in the DNA vaccinated mice indicating a Th2 type of immune response. The peptide immunized mice showed a mixed Th1/Th2 immune response with IgG1 and IgG2a antibodies in similar amounts. The characteristic Th2 type of response after  $A\beta$ 42 DNA vaccination reduces the likelihood of inflammatory activities of the immune system towards the self-peptide  $A\beta$ 42 in brain. Therefore, this vaccination protocol has a high probability to be effective and safe for treatment therapy in AD.

#### *Repair strategies in multiple sclerosis* M. Rodriguez

Current treatments for multiple sclerosis (MS) assume that the immune system destroys oligodendrocytes and axons. Some lead to a partial clinical response, but many patients progress to severe, permanent disability. To induce a sustained response, targeting oligodendrocytes, neurons, and axons, CNS cells that play a critical role in the disease process, was proposed. Current experimental therapies target these cells to activate oligodendrocytes to produce new myelin or activate neurons to extend their processes. They discovered that natural autoantibodies in the serum of healthy individuals contain immunoglobulins directed against surface molecules on oligodendrocytes. One antibody, HIgM22, produced dramatic remyelination in various animal models of MS apparently by acting against integrins on the cell surface of oligodendrocytes. The antibody binds to lipid rafts on oligodendrocytes to induce a calcium influx through an alpha-amino-3-hydroxy-5-methyl-4 isoxazolepropionic acid (AMPA)-mediated channel, resulting in phosphorylation of specific remyelination-inducing molecules. Both HIgM12 and HIgM42, also discovered, apparently targeted sialidase-containing compounds on gangliocytes. These antibodies induce neuron outgrowth. Recent experiments in mice chronically infected with Theiler's murine encephalomyelitis virus

# HIGHLIGHTS FROM INTERNATIONAL NEUROSCIENCE MEETINGS

(TMEV), a model for human MS, demonstrate that the remyelinating antibody (HIgM22) and the neurite-binding antibodies (HIgM12 and HIgM42) enter the CNS of animals to reverse dramatically persistent neurological deficits. Recombinant HIgM22, generated in large quantities in a good manufacturing practice (GMP) facility, targets injured areas of CNS and promotes maximal remyelination within 5 weeks after a single low dose (25 microg/kg). Unlike current therapies for MS aimed at treating inflammation, remyelination-promoting antibodies induce tissue repair within the CNS at sites of damage on the myelin-synthesizing cells. The goal is to initiate a long-term reparative effect on the CNS.

## *Scientific presentations*

### *Epilepsy highlights*

- Epilepsy during pregnancy and antiepileptic drug-induced teratogenesis was discussed. Avoidance of Valproate in pregnancy and in women within the childbearing age, due to substantial risk of cognitive impairment, was highly recommended.
- There is ongoing active research on the pharmacogenomics of epilepsy in order to: understand the genetic basis of multi-drug resistant epilepsy, antiepileptic drug-induced teratogenesis, and the development of new antiepileptic drugs.
- Researchers in Germany showed that the novel drug Lacosamide is effective in a considerable number of patients with difficult to treat focal epilepsies. No severe side effects were observed.

### *Stroke highlights*

- New non-invasive imaging techniques (functional TCD, carotid duplex) to enable rapid evaluation of the carotid system to detect potential treatable carotid stenosis.
- An analysis of 40155 patients with acute ischemic stroke from the Danish Registry found that very early mortality was first determined by stroke subtype and stroke severity, and to a lesser degree by heart disease and age.
- A multicenter randomized double blind study from China showed that dl-3n-butylphthalide (NBP) injection is an effective treatment in acute cerebral infarction.
- Researchers from the University of Minnesota showed that aggressive systolic blood pressure reduction using intravenous nicardipine was well tolerated with low risk of hematoma expansion, neurological deterioration, and in-hospital mortality in patients with intracerebral hemorrhage.
- Researchers showed that cerebral angiographic features can distinguish reversible cerebral vasoconstriction syndrome (symmetric, segmental, “sausage on a string” appearance) from primary angiitis of the CNS (irregular, “notched” appearance).
- More compelling evidence of the benefit of neuroprotection in acute ischemic stroke.
- Several presentations confirmed that hyperglycemia is a risk factor for poor outcome in patients with intracerebral hemorrhage.

### *Multiple sclerosis highlights*

- Recent evidence has witnessed renewed and intensified interest in the complex genetics of MS. Advances in pharmacogenetics and pharmacogenomics have led to investigation therapies tackling multitudes of modalities of therapies
- Researchers have identified 2 gene variations that are resistant to interferon  $\beta$  (IFN- $\beta$ ) therapy. This finding could lead to a biomarker for determining when IFN- $\beta$  is appropriate for the treatment of MS.
- Multicenter studies from Europe and United States showed good efficacy and safety of natalizumab treatment in relapsing MS.
- A phase III double-blind placebo-controlled study from United States and Europe provided evidence for the use of cladribine oral tablets for relapsing-remitting MS.
- Researchers from Italy report a high incidence of acute leukemia in MS patients treated with mitoxantrone.
- The addition of methylprednisolone to IFN- $\beta$  therapy may reduce disease activity in patients with MS to a greater degree than treatment with IFN- $\beta$  alone.

### *Neuromuscular diseases highlights*

- Newer treatments, such as gene therapy, are being studied in Duchenne muscular dystrophy with promising results.
- New updated guidelines for the management of myasthenia gravis and chronic inflammatory demyelinating neuropathies.

# HIGHLIGHTS FROM INTERNATIONAL NEUROSCIENCE MEETINGS

## *Headache/Pain highlights*

- A large, phase III clinical program evaluating botulinum toxin type versus placebo as headache prophylaxis in 1384 adults provides level one evidence of the effectiveness of botulinum toxin type A for headache prophylaxis in adults with chronic migraine.
- Two randomized, double-blind, placebo-controlled clinical trials showed that the oral calcitonin gene-related peptide (CGRP) receptor antagonist Telcagepant is effective in the acute treatment of migraine.
- A common cause of headache is overuse of headache medications. These headaches are difficult to treat once they occur, since withdrawing all medications often makes the headache even worse. A study showed that patients who took prednisone for 5 days during withdrawal had headaches that lasted only half as long as those who received no treatment. This therapy may help patients with medication-overuse headaches attempt to stop using headache drugs.
- New treatment options for pain caused by diabetic peripheral neuropathy: while oral medications from 2 different drug classes appear effective, injection of botulinum toxin does not.

## *Other highlights*

- *Sleep disorders:* Several presentations confirm that sleep disorders are common in persons older than 70 years, in patients with mild traumatic brain injury, in patients with Parkinson's disease, and in patients with ischemic cerebrovascular disease.
- *Oncology:* Temozolomide chemotherapy plus radiation is superior to radiation alone in treatment of glioblastoma multiforme, according to a new study. Six weeks of treatment led to a better than two-fold increase in survival of patients 2 years later, which translated into a 37% reduction in risk overall from this deadly and difficult-to-treat form of brain cancer.
- *Alzheimer's dementia:* Researchers from Germany showed in a phase II study that BAY 94-9172 positron emission tomography had a specificity of 90% for the detection of cerebral beta-amyloid plaques. This is consistent with the results of studies where the clinical diagnosis of Alzheimer's disease was compared with the definitive post-mortem histopathological diagnosis.

### CONSULTANT NEUROSURGEON

Candidates should possess a Standard International qualification in Epilepsy Surgery. Should have at least 3-5 years experience as a Neurosurgeon.

---

For interested applicants, please send detailed curriculum vitae, 3 references, copies of professional qualifications, and passport photo, by post or by fax to:

#### Department of Neurosciences

Riyadh Military Hospital, PO Box 7897, Riyadh 11159, Kingdom of Saudi Arabia.  
Tel. +966 (1) 4777714 Ext. 25397. Fax. +966 (1) 4762980. E-mail: [alnizama@yahoo.com.uk](mailto:alnizama@yahoo.com.uk)

#### Recruitment Manager

Riyadh Military Hospital, PO Box 7897, Riyadh 11159, Kingdom of Saudi Arabia.  
Tel. +966 (1) 4777714 Ext. 5426. Fax. +966 (1) 4779179. E-mail: [www.rkh-hr.com](http://www.rkh-hr.com)