10th ASEAN Neurological Association (ASNA) Biennial Convention (Part II)

The ASEAN Neurological Association (ASNA) was formed in 1994 and at that time consisted of five member countries; Indonesia, Malaysia, Philippines, Singapore and Thailand. Presently, there are 10 members consisting of the member nations of Association of South East Asian Nations (ASEAN). The main aim of the association was to bring together experts and clinicians involved in the care of neurology from the ASEAN regions to discuss and share their knowledge and research findings. It also provide good opportunities to collaborate and form friendships. The official journal of the ASNA is the Neurology Asia which is being published quarterly and is available online from the journal website (www.neurologyasia.com).

The first ASNA convention was held in Manila, Philippines in 1995. The convention has since been organized biennially with the second convention held in Singapore (1997), followed by Chaingmai Thailand (1999), Kuala Lumpur, Malaysia (2001), Cebu, Philippines (2003), Jakarta, Indonesia (2005), Cha-am, Thailand (2007), Kuala Lumpur (2009) and Bali, Indonesia (2011).

The 10th Convention, ASNA 2013 being held in Bandar Seri Begawan Brunei Darussalam consisted of two day plenary lectures and symposium. This was preceded by a day of workshop. This convention brought together experts from member nations and also from non member nations.

Research findings were also presented as posters in the poster sessions. For the full programme and the abstracts presented, please refer to the Brunei Int Med J. 2013; 9: Supplement 1 available from the journal website at *www.bimjonline.com*.

Day 1 Convention

Plenary 3: Movement disorders: In this session, a talk entitled '***Palliative care for patients with Parkinson's disease***' was delivered by *Janis Miyasaki* (Toronto, Canada), a renowned expert in movement disorders, and a master in the use of botulinum toxin for the management of movement disorders.

The goal of any palliative care is to achieve the best quality of life for patients with incurable disease, including Parkinson's disease. In patients with Parkinson's Disease, a progressive neuro-

degenerative disease where patients' cognitive function remains intact in the initial phase and patient can experience debilitating symptoms and depression. Cognitive decline eventually follow. In the care of patient with Parkinson's disease, the principles of palliative care should be applied throughout the course of the disease and should not be limited to the terminal phase of the disease. The main focus of palliative care is to focus on prevention and relief of suffering through anticipation and early identification, assessment and treatment of any pain or other physical, psychological and spiritual problems. Unfortunately, the needs of patients with Parkinson's disease are not always identified and disease progression makes intervention less effective. As a result patient becomes more disabled and dependent. The palliative phase can be identified by the inability to tolerate adequate dopaminergic therapy, unsuitability for surgery or the presence of advanced comorbid conditions. Palliative care for patients with Parkinson's disease involve clinicians, nurse, carers or family, institutions such as nursing homes or hospice.

Symposium 5: Neuro-Infectious disease

This symposium discuss on some of the common infections that affect the nervous system. The first talk by *Tunlayadechanont S* (Thailand) entitled '***Some specific nervous system infections in the tropics***' looks at infections commonly encountered in Southeast Asia. Infections are treatable and hence important to be familiar with infections that affect the nervous system in our own local setting. Any delay in initiation or untreated can lead to significant neurological impairment and even death. *Streptococcus suis* may be the most common cause of adult bacterial meningitis in some ASNA countries. Tetanus remains common in some countries and without any laboratory testing, the diagnosis and management requires clinicians to be aware and always consider it in the differential diagnosis. The speaker also touched in infections such as Cysticercosis and Gnathostomiasis which can cause variable clinical signs and symptoms. These infections can affect any part of the nervous system and management also depends on the number, locations and viability of the organisms. Unfortunately, there is no formal training in neurological infection which is suitable to all regions. The speaker highlighted that sharing of knowledge on these specific nervous system infections is importantly and clinicians need to aware of what is common in their setting. Tuberculosis was not covered in this talk as it will be covered in another talk in the same symposium. The second talk '***Viral meningoencephalitis: Emerging life threatening burden worldwide***' by *Prof. Uta Meyding-Lamade* (Frankfurt, Germany, National Stroke Rehabilitation Centre, Brunei) discuss on the common and less common viral infections affecting the central nervous system. The most common manifestation of viral infection of the nervous system is meningitis. In most instances, most are self limiting. Common symptoms include headache and fever which will spontaneously resolve in 90% of cases. Viral meningoencephalitis frequently presents with a biphasic course; a prodormal phase (fever, headache, flu like symptoms) followed by disturbance of consciousness, focal neurological manifestations and seizures. A number of viruses can cause meningoencephalitis and manifestations can vary. Diagnostic workup needs to be thorough and treatment is best provided by specialists in this field in neurological unit. The authors touched on several viruses. Japanese encephalitis (JE) is endemic to the tropic and is a disease that can be prevented with vaccination. Dengue infection which is also endemic to Brunei is a common cause of neurological manifestation. Chikungunya, Nipah and Hendra virus infections affect mainly the South Asian region (Indian subcontinent). The most common vector for these viruses is the mosquito. With globalisation and climate change, spread of these infections can occur and clinicians need to be aware of these viral causes of meningoencephalitis. This topic was particularly relevant as Brunei had an outbreak of viral meningoencephalitis in 2013. *Dr AR Ganiem* (Bandung, Indonesia) spoke on '**Meningitis: Aetiology and Management in the ASEAN region'**, an important topic for neurologists working in the region. He briefly touched on the features of meningitis; clinical manifestations (fever, headache, de-

creased level of consciousness, and neck stiffness) and categorisation into acute, subacute or chronic meningitis which all clinicians should be aware of. Chronic meningitis can be more difficult to recognise. Meningitis is not restricted to a region and can be seen anyway in the world. However, it is important to be aware and be familiar with aetiologies are usually unique to a region. It is well known that the causative agents vary according to the type of meningitis and the age of patients. The ongoing HIV epidemic has contributed to the shift in the epidemiology but this is more evident in countries that are more affected such as Thailand. Causes that clinicians need to be aware apart from the commonly known causes include Tuberculosis and Cryptococcus. In the tropic, clinicians also need to consider melioidosis especially in patients with risk factors (i.e. poorly controlled diabetes mellitus, end stage renal disease and hematological disorders). On the management from, there are standardized therapies for Cryptococcus but for tuberculosis, the management of tuberculosis meningitis remains not so well established. Apart from using standard anti-tuberculous therapy, the role of steroid and other studied medications remain undefined. Dexamethasone reduces mortality associated with tuberculous meningitis in the first two years and recent evidence suggests that genetic variation may play an important role in the response to this drug. Promising approach include increasing the dose of rifampacin and or adding fluoroquinolones in the current regime. The role of neurosurgery needs to be further explored. The last speaker for this symposium, *S Chankrachang* (Thailand) touched on '***CNS tuberculosis'***, an infection that remains endemic in the Southeast Asian region. CNS tuberculosis accounts for approximately 1% of all infections caused by mycobacterium but the morbidity and mortality of CNS tuberculosis is high. Tuberculous meningitis is the most common form of CNS tuberculosis and is characterised by a slow progressive granulomatous inflammation of the basal meninges which lead to hydrocephalus, brain infarction and death. Meningitis commonly develops as a complication of post primary infection in infants and children and from reactivation of latent infection in adults secondary to immune deficiency. The pathogenesis of CNS tuberculosis involve dissemination of the organism during bacteremia resulting in scattered tuberculous foci or tubercles in the brain, meninges, or adjacent bony structures. Rupture of subependymal tubercles into the subarachnoid space leads to development of tuberculous meningitis. The management of CNS tuberculous are often faced with obstacles such as late presentation or case detection, lack of rapid, accurate and cost effective laboratory diagnosis and even the therapy. With the increase in multi-resistant cases and co infections with HIV, successful management remains difficult.

Symposium 6: Movement disorders

The first talk in this symposium was delivered by *Lim SY* (Malaysia) who talked on '***Non-motor symptoms of Parkinson's disease***'. Apart from the well-known and disabling motor symptoms (bradykinesia, tremors and rigidity), patient with Parkinson's disease experience a multitude of other symptoms that are common to many other chronic diseases and they are equally disabling. In this talk, a broad framework on how to approach the non-motor symptoms of Parkinson's disease discussed. This frameworks categorizes the symptoms or manifestations into a) neuropsychiatric, b) autonomic, iii) sleep related, and iv) pain/sensory. Depression or mood disorders are common and may go unrecognized as patients may not be able to express their concern properly due to the Parkinson's disease. Autonomic manifestation is part of the Steele Richardson and is not uncommon in the other types of Parkinson's disease given the age of patients and the multiple comorbid condition and the medications prescribed. Therefore, it is not surprising that sleep disorders is common. PD related psychosis, impulsive-complusive behaviors (ICBs), and non-motor fluctuation were covered in more detail. The audience was also updated on the more important developments in the management of Parkinson's disease; epidemiology, the use of Braak staging scheme, management strategies and the effects of deep brain stimulation (DBS) and infusional therapy. The Braak Staging scheme (developed by Heiko

Braak 2003) refers to the methods to classify the degree of pathology. Based on this scheme, Lewy bodies first appear in the olfactory bulb, medulla oblongata and pontine tegmentum, individuals at this stage being asymptomatic. As the disease evolves, Lewy bodies later attain the substantia nigra, areas of the midbrain and basal forebrain, and finally reach areas of the neocortex. DBS is a surgical procedure used to debilitating symptoms of Parkinson's disease (PD), such as tremor, rigidity, stiffness, slowed movement, and walking problems. At present, the procedure is used only for patients whose symptoms cannot be adequately controlled with medications. A surgically implanted neurostimulator, approximately the size of a stopwatch deliver electrical stimulation to targeted areas in the brain that control movement. This blocks the abnormal nerve signals that cause tremor and PD symptoms. The next talk was delivered by *Jamora RD* (Philippines) on '***Updates on Dystonia'***. Dystonia defined as abnormal movement that is characterised involuntary, patterned and often repetitive muscle contractions of opposing muscle groups resulting twisting or abnormal posturing. Dystonia was previously classified based on the age of onset (</> 26 years), distribution of abnormality (focal, segmental, multifocal or generalized), clinical features (continuous or fluctuating), and the underlying aetiology (primary, secondary, dystonia plus or heredodegenerative [Inherited disorders characterized by progressive atrophy and dysfunction of anatomically or physiologically related neurologic systems]). Recently a new classification has been proposed and the new scheme identifies two distinct axes; clinical features and aetiology. The clinical caharacterisitics describe the phenomenology of dystonia and the aetiology is dynamic but includes identifiable anatomical changes and pattern of inheritance. The speaker also touched on the LuBags disease, a X-linked dystonia-parkinsons that is endemic among males from the Philippines. The last talk of the symposium by *R Bhidayasiri* (Thailand) was on '***Infectious diseases and movement disorders***'. Unknown to non-neurologist clinicians, infectious disease can cause a large variety of movement disorders. Viral, bacterial, fungal and parasitic agents all can cause direct compromise of the motor system (extrapyramidal system) or indirectly through molecular mimicry leading to acquired autoimmune mediated movement disorders. However, it is not uncommon, multiple mechanisms are involved. A good example of infectious disease leading to movement disorder if with HIV/AIDS where hemichorea-hemiballism is not uncommonly encountered manifest through direct involvement by opportunistic infections while opsoclonus-myoclonus syndrome develop as part of an immune reconstitution syndrome. Many other movement disorders such as Sydenham's chorea or associated with encephalitis lethargica are now believed to be immune mediated through detection of antineuronal antibodies. Like the previous movement disorder session, interesting video were presented.

Plenary 4: Autoimmune epilepsies

Epilepsy is a common neurological condition with a varied disease spectrum that can be difficult to manage. With the increase in the understanding and discoveries of novel neural autoantibodies, an immune-mediated cause of epilepsy is increasingly being identified in a subsets of patients with epilepsy. The talk entitled '***Autoimmune mediated Epilepsies***' in this plenary session was delivered by *Dr Amy Quek* (Singapore). Some of these patients may be difficult to manage with standard antiepileptics. The underlying autoimmune pathogenesis identify this group as being amendable to immunotherapy. Discoveries of antibodies against neuronal surface antigens had led to improvement in the understanding of this entity. Autoimmune epilepsy can be classified into: a) Epilepsy syndromes (e.g. Rasmussen's encephalitis, Landau-Kleffner syndrome, infantile spasm and Lennox-Gastaut syndrome), b) Epilepsy associated with other immunologically mediated diseases (SLE and Hashimoto's encephalopathy), and c) common unselected groups with antibodies (e.g. antiphospholipid, antinuclear, antiganglioside, and antiglutamic acid decarboxylase). There is currently no standard guideline available for diagnosis of autoimmune epilepsy. However, the presence of the following features may indicate the autoimmune epilepsy: seizure onset correlating

with autoimmune disease exacerbations, seizure onset or breakthrough seizures associated with acute CNS causes damage (i.e. head injury, stroke and infections), failure to control despite multiple antiepileptic drugs, and childhood febrile convulsions that later develops into temporal lobe epilepsy. There are numerous possible neuronal autoantibodies that could indicate autoimmune epilepsy; i.e. antiphospholipid, antinuclear, antiganglioside, antiglutamic acid decarboxylase, anti-GluR3, and antimitochondrial. Pathological examination of brain tissue from individuals with focal epilepsy that has not responded to other treatments: finding of (scarring) gliosis is consistent with a chronic inflammatory state. Autoimmune epilepsy is mainly diagnosed by clinical history. When immunomodulation therapy is planned autoantibody testing may help to improve the clinical responses. The management of autoimmune epilepsy is still not standardised. Traditional antiepileptic medications, Vagus nerve stimulation (VNS) and surgical treatments along with immunomodulatory agents such as steroids and ACTH and intravenous immune globulin have the potential to produce significant improvements in refractory epilepsy.

Plenary 5: Neuro-Infectious Disease

This plenary session with the talk entitled '***Sacrocystosis, an emerging muscle infection***' by *Tan CT* (Malaysia) touched upon an interesting infection is unknown to most. In this talk, the speaker described their experience with sacrocytosis infection. Sacrocytosis affecting the human musculature is considered rare. However, reported figures represent gross underestimate of the human burden of disease. A study of 100 human tongues obtained at post mortem in Malaya revealed an infection rate of 21%. There was no sex difference and the age range was 16 to 57 years (mean 37.7 years). Stool examinations in Thai labourers reported a prevalence of ~23% with virtually all cases to be asymptomatic. Sacrocytosis affecting human is also thought to be largely asymptomatic. However, there are reports of febrile myalgic illness among tourist returning from island holiday in Malaysia. The speaker described in more detail their experience with an outbreak of sacrocytosis in 2012 that involved 89/92 (97%) campers returning from Pulau Pangkor. Those who were affected developed relapsing fever and myalgia. In 10%, there was distinctive myositis of the jaw muscles with facial swelling. Muscle biopsy identified leading to the diagnosis of sacrocytosis. The patients were treated symptomatically with anti-inflammatory medications as there were no specific treatment available. Investigations led to the discovery of contaminated water source from the hill, which was collected and used for washing.

Plenary 6: Neuromuscular Disease

The talk in the plenary session was on ***'Guillain Barré syndrome: Pathogenesis and action mechanism of immunotherapy'*** delivered by *Nobuhiro Yuki* (Singapore), the man who pioneered and reported the immunological mechanism of Guillain-Barré syndrome (GBS). GBS is characterised by limb weakness and areflexia, is the prototype of postinfectious autoimmune diseases, and *Campylobacter jejuni* is the most frequent antecedent pathogen. GBS subsequent to *C jejuni* enteritis is associated with a severe, pure motor axonal variant and IgG antibodies against GM1, GM1b, GD1a, or GalNAc-GD1a, gangliosides expressed in human peripheral nerves. Lipopolysaccharides of *C jejuni* isolated from GBS patients have ganglioside-like epitopes. Fisher syndrome (FS), characterised by ophthalmoplegia, ataxia, and areflexia, is a GBS variant associated with anti-GQ1b IgG antibody. GQ1b is enriched in the cranial nerves that innervate the extraocular muscles. Some patients develop FS after *C jejuni* infection, and the lipopolysaccharide present bears the GQ1b epitope. Molecular mimicry is a possible cause of GBS and FS. Yuki journey if GBS started when he encountered a patient who developed GBS subsequent to *C. jejuni* enteritis. Contrary to what he had learnt as a student that GBS was associated with a good prognosis and involves demyelination, this particular patient had a poor outcome, and electrophysiology suggested axonal degeneration not demyelination. Inspired by a paper from Norman Latov and co-workers, he and his colleagues showed a close association of

of axonal-subtype GBS after *C jejuni* enteritis with IgG autoantibodies to GM1 ganglioside. They also identified molecular mimicry of GM1 and lipo-oligosaccharides of *C jejuni*, and established a model of GBS. This talk also touched on the role of intravenous immunoglobulin (IVIG) therapy. Currently IVIG is the first line treatment for GBS. IVIG is known to have several modulatory effects on the immune systems, but the specific mechanisms that facilitate recovery in GBS are not well characterised. A number of possible mechanisms have been suggested. IVIG protects nerves from anti-ganglioside antibody-mediated injury; neutralisation of autoantibodies and inhibition of complement activation are two major mechanisms. This also results in the inhibition of pro-inflammatory cytokines. Prof. Yuki's research journey in GBS is described in detailed in a recent review 'Guillain-Barré syndrome and anti-ganglioside antibodies: a clinician-scientist's journey' he authored, published in the Proc Jpn Acad Ser B Phys Biols Sci. 2012; 88:299-326 (available online at *https://www.jstage.jst.go.jp/article/pjab/88/7/88_PJA8807B-01/_pdf* or the PubMed Central at *http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3422685/).*

NOTE: Some materials not covered in the lecture presentations have been added into the summary for benefits of the general readers.

The third part of the Convention report will be published in the April 2014 issue of the Brunei International Medical Journal.