4th International Congress on Neurology and Epidemiology

Kuala Lumpur, Malaysia, November 6–8, 2014

Abstracts

Editors

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The Long-Term Prognosis of Epilepsy and the Development of Refractory Epilepsy

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Epilepsy is a chronic clinical condition characterized by repeated unprovoked seizures. In newly diagnosed patients, the outcome of the disease is mostly favourable, with remissions in up to 90% of cases. In newly diagnosed patients, a satisfactory response to the initial treatment can positively affect the early prognosis of the disease. However, the long-term outcome of epilepsy is apparently unaffected by early treatment, suggesting that the response to early treatment does not necessarily affect the long-term prognosis of epilepsy. Early remission does only indicate that the disease runs a mild course, which is predicted by seizure control after treatment start. However, more recent studies done on the long-term prognosis of epilepsy found that seizure outcome is more complex and follows differing patterns. In a population-based study of patients with onset of seizures as children and followed for an average period of 37 years (Sillanpaa and Schmidt, 2006), the course of the disease was predicted by the response to early treatment only in some cases and five main patterns could be recognized: 1. Early remission within the first year of treatment continuing to terminal remission (16% of cases); 2. Late remission after the first year of treatment continuing to terminal remission (32%); 3. Relapsing-remitting course, which re-enter remission following a relapse after an early or late remission (19%); 4. Worsening course, which does not re-enter remission following a relapse after an early or late remission (14%); 5. Drug-resistance ever (19%). Other reports confirmed in part these findings and showed that patients found to be drug resistant by history could still attain seizure control after treatment changes. Thus, drug-resistant epilepsy can be better interpreted as a dynamic process, predicted by patient’s and disease characteristics, timing and type of drug treatment.
Epilepsy is a chronic neurological disease with a worldwide incidence ranging from 16 to 111 per 100,000 per year and a prevalence ranging from 2.2 to 41 per 1,000, with the highest rates reported in developing countries. Epilepsy affects all ages, with peaks in the two extremes, and both sexes, with a slight predominance in males. Patients with epilepsy are at increased risk of death compared to the general population, with a standardized mortality ratio ranging from 1.6 to 4.1. The burden of epilepsy in the world has remained stable in the last decades because of the incidence, prevalence and mortality of the disease have been reported unchanged both in developed and in developing countries. However, the burden of the disease is going to increase in the next future for two main reasons, one real and the other artifactual. Given the peak of the disease in the elderly, we expect that with the worldwide aging of the population the incidence of the disease is going to increase. However, an increase is also expected in light of the new definition of the disease proposed by the International League Against Epilepsy. Along with patients experiencing at least two unprovoked seizures (the ones included in almost every epidemiological study on epilepsy), patients with only one seizure will be included if a 60% or higher chance of relapse can be estimated. With reference to the management of the disease, nothing is new because the available compounds, even the ones most recently marketed, have fairly similar efficacy and tolerability profiles. The future of the treatment of epilepsy will be the discovery of drugs with novel mechanisms of action having antiepileptogenic effects. In contrast, the epidemiology of migraine has benefited from the introduction of the ICHD-II, which has been invariably used in the most recent studies. On this basis, the aggregate weighted estimates of the 12-month prevalence are 11.5% for definite migraine and 7% for probable migraine. An increasing amount of data has been obtained in children (12-month prevalence, 10.1% and 1.6% respectively for definite and probable migraine). Migraine is the neurological disorder with the greatest health care costs. Migraine has a favorable prognosis in most children and adults. Less than 50% of migraine sufferers in the general population receive treatment. With few exceptions (selected non-pharmacological treatments), nothing is new in the management of migraine.
Desmoteplase is essentially inactive unless fibrin is present as was its highly fibrin-selective nature when compared with t-PA. This was welcome finding, the net clinical benefit of desmoteplase would be devoid of the unwanted side-effects inherent with t-PA and on this reasoning, would have a reduced risk at causing sICH. A series of clinical trials have been undertaken to evaluate desmoteplase in selected patients with AIS. The recently completed DIAS-3 trial confirmed that desmoteplase has a favourable safety profile as the rate of sICH in AIS patients was comparable to placebo when administered with the 3 to 9 h time frame post-stroke onset at currently pursued therapeutic dose. While this was welcome finding, the net clinical benefit of desmoteplase still has to be properly analysed and evaluated. While a more detailed account of DIAS-3 is eagerly awaited, desmoteplase has at least revealed that thrombolysis and sICH can be uncoupled and that thrombolysis beyond the current restricted time-frame is still an open possibility.

Tissue-type plasminogen activator (t-PA)-induced thrombolysis for patients with acute ischaemic stroke (AIS) occurs for just a fraction of eligible patients as t-PA can only be administered within 3 or 4.5 h (depending on country) post-stroke onset. This restricted time window is based on the risk profile of t-PA at promoting symptomatic intracranial haemorrhage (sICH) and its reduced clinical benefit when used outside of this time frame. There has been a need to develop safer thrombolytic agents that do not promote the risk of sICH and which can be used over an extended time frame. Desmoteplase, a plasminogen activator originally derived from the saliva of the common vampire bat, desmodus rotundus, was put into clinical development for patients with AIS over a decade ago. The justification for its development was its highly fibrin-selective nature when compared with t-PA. Desmoteplase is essentially inactive unless fibrin is present as a cofactor to allow it to activate plasminogen into its active form, plasmin. The relative inability of desmoteplase to activate circulating plasminogen would significantly reduce bystander effects seen with t-PA. While this has been a valid argument, what has come to light in recent years is that t-PA has non-fibrinolytic effects in the brain that could not have been foreseen, including its ability to modulate neuronal activity, promote neurotoxicity and to increase blood brain barrier (BBB) permeability; the latter effect being arguably the most important non-fibrinolytic feature of t-PA as this likely precedes its capacity to induce ICH. A critical question was whether desmoteplase also harboured any of the non-fibrinolytic features seen with t-PA. In 2003, laboratory based studies first showed that desmoteplase was incapable of promoting neurotoxicity, even when evaluated in mouse models at 100-fold higher levels than t-PA. More recently, using an in vitro model of the BBB, we reported that t-PA promoted BBB permeability under both normoxic conditions and under oxygen-glucose deprivation (OGD) whereas desmoteplase had no effect at all, even in the presence of both plasminogen and fibrin. It was concluded that t-PA was initiating BBB opening via cell-surface receptors on astrocytes that were not shared with desmoteplase (Freeman et al Brain Res 2014). These findings strongly suggested that desmoteplase would be devoid of the unwanted side-effects inherent with t-PA and on this reasoning, would have a reduced risk at causing sICH. A series of clinical trials have been undertaken to evaluate desmoteplase in selected patients with AIS. The recently completed DIAS-3 trial confirmed that desmoteplase has a favourable safety profile as the rate of sICH in AIS patients was comparable to placebo when administered with the 3 to 9 h time frame post-stroke onset at currently pursued therapeutic dose. While this was welcome finding, the net clinical benefit of desmoteplase still has to be properly analysed and evaluated. While a more detailed account of DIAS-3 is eagerly awaited, desmoteplase has at least revealed that thrombolysis and sICH can be uncoupled and that thrombolysis beyond the current restricted time-frame is still an open possibility.

There is a huge burden of stroke in developing countries particularly in Asia. A significant proportion of the patients with stroke are below 49 years of age in these regions. Reliable good
quality data on stroke epidemiology is limited due to availability of health infrastructure, human resources and funding. Door-to-door survey method has been used in few studies from developing countries. WHO STEPS approach has been adapted widely in many developing countries. There is good quality studies available from India based on WHO STEPS methodology. The collection of mortality data is problematic because of poor documentation of deaths in these nations. Verbal autopsy has been used in many studies to capture this vital information. It is also difficult to gather information from patients who take treatment from outside the study area. The Indian Council of Medical Research (ICMR) supported the recently concluded population based stroke registry in Ludhiana city, northwest India under the Task Force Project. The feasibility phase of this project revealed many practical problems in carrying out this study. Locally applicable solutions were implemented in documentation of deaths, patients receiving treatment outside the field of study and in collection of data from general practitioners and scan centres. In developing countries while designing an epidemiological study in stroke a feasibility phase should be incorporated to study the practical difficulties at the field level. Based on the pilot phase measures could be taken to obtain accurate information. Despite all the obstacles more and more data is emerging from developing countries in the recent years.

References


PS5 – Selected Aspects of Neuroepidemiology of Stroke and Epilepsy – 1

PS5-1
Environmental Factors and Stroke Occurrence from Sciences to Practice

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Stroke is a major public health problem emerging both in high and low income countries.

Classical vascular risk factors account for 90% of strokes [1]. While there is accumulating evidence for a triggering effect of short-term environmental parameters on stroke risk in patients with vascular risk, there are some robust data regarding the direct effect of environmental factors on stroke occurrence [1], even if remaining a matter of controversy [1, 2]. Environmental factors gather factors linked to ground, water, air, food and drink pollution. The action of radon provided by ground and nitrates by water, have no known vascular impacts. Glucose and lipids in food and drinks have a well-known, direct role on atheroma. To the opposite, environmental factors begin to emerge as major risk factors by the way of 3 actions: role of weather (ambient temperature, relative humidity, atmospheric pressure) and geomagnetic activity [1]. The role of cold weather on stroke occurrence, the role of hot weather on Transient Ischemic Attack the role of ozone pollution [3] are all associated with increased risk of stroke. Geomagnetic storms (earth’s magnetic field) should be considered along with other established risk factors because they are associated with increased risk of stroke [1].

Contrary to that observed in the western countries, there has been a substantial rise in the incidence of stroke in India over the past four decades. According to the current population-based data, the incidence rate of stroke is 135 to 152 per 100,000 persons and one-month case fatality rate 27 to 41 percent. Socio-economic transition in the country with consequent lifestyle changes coupled with inadequate control of the principal risk factors has lead to this enormous increase in stroke incidence. In at least 70 percent of Indians, hypertension remains either untreated or inadequately treated. Indians are genetically predisposed to type 2 diabetes and many are also unaware about its proper treatment. Smoking continues to be prevalent in 20 percent and tobacco chewing in 40 percent of the population. High lipoprotein(a), borderline high LDL cholesterol and significantly low HDL cholesterol make the Indians at risk of developing severe atherosclerosis at an earlier age. Spreading awareness and adequate control of the above risk factors, healthy diet with lowering of dietary salt intake and physical exercise are the core preventive measures of stroke that need to be implemented. Most of the stroke related death in India occurs within the first 7 days. The reasons include delay in hospitalization, poor access to thrombolytic therapy and dearth of comprehensive stroke care units. Since out of pocket expenditure for health is 20 to 80 percent of total expense, stroke survivors with disability impose enormous financial, physical and psychological burden upon their family members, particularly if they are financially less well off. About one third of the disabled stroke survivors resort to alternative medicines because of non-affordability of allopathic drugs. Hence in a developing country like India, emphasis should be more on the preventative aspects of stroke. In 2008 the Government of India has launched the National Health ...
Essential tremor (ET) is one of the most prevalent neurological diseases, with a prevalence (all ages) = 0.9%. Prevalence increases markedly with age, and especially with advanced age (e.g., 6.3% among individuals age 65 and older, and as high as 21% among people age 95 and older). Despite its high prevalence, ET is among the most poorly understood and most commonly misunderstood neurological disorders. This talk highlights several recent advances in our understanding of the epidemiology of ET. In order to better appreciate these advances; however, one must have some knowledge of recent developments/changes in the underlying conceptualization of the disorder, including shifts in our thinking about both its clinical features and its underlying biology. Although viewed in the past as a clinically-bland, monosymptomatic entity, more rigorous clinical research over recent years indicates that ET is characterized by a variety of motor as well as non-motor features. These motor features include not only a range of tremors but also gait abnormalities. The non-motor features include cognitive changes (ranging from mild to severe), apathy, depression, and changes in sleep. Indeed, the notion is forming in the literature that ET may be a family of diseases perhaps better referred to as the ‘essential tremors’. The underlying biology of ET is not well understood. In the past, the disorder was viewed as a physiological disarrangement due to abnormalities in olivary-cerebellar circuits. However, there are few if any empirical data to support this somewhat outdated disease model. More recently, and based on controlled postmortem studies, the disease is being regarded as perhaps one of cerebellar degeneration. As noted above, the epidemiology of ET has seen advances in recent years. One major shift has been an increase in our understanding of the links between ET and other degenerative disorders, including Parkinson’s disease, Alzheimer’s disease, and progressive supranuclear palsy. There is reasonable epidemiological evidence to support links between ET and these neurodegenerative diseases. A second shift lies in the domain of environmental epidemiology. Several toxic/environmental etiologies have been studied, including harmene (1-methyl-9H-pyrido[3,4-b]indole), a beta-carboline alkaloid with tremor-producing properties. Studies in both New York and Spain have established associations between higher blood and brain concentrations of this dietary toxin and ET. As such, harmene could be the first identified modifiable risk factor for ET. In summary, ET is a common disorder, which has eluded our understanding, yet we have seen a recent maturation in our understanding of the clinical and biological features of this disorder. Along with this have come several important advances in our understanding of the possible environmental causes of this disorder and its relation to other neurodegenerative diseases.
given adequate support and training to care for the stroke survivors once they return home. Consequently, caregivers often experience stress and negative health consequences that can additionally contribute to poor long-term rehabilitation outcomes and threaten the sustainability of home care. One way of improving support may be to provide relevant audio-visual information in DVD format. Currently, we are conducting research on the effectiveness of doing this. Improving support for families is particularly important in light of research on long-term recovery from stroke that reveals that while some individuals continue to make functional gains months and years post-stroke, many others become increasingly dependent on their families. This suggests a need for the third strategy namely, the need for ongoing community-based support. Community-based rehabilitation involve the combined efforts of people with disabilities, their families and communities, and the appropriate formal services such as health, social, welfare, vocational and education. Community-based rehabilitation may have many advantages including maintaining and perhaps even increasing self-efficacy and providing family support which would contribute to the sustainability of the recovery that has already occurred during the acute rehabilitation phase as well as the continuation of home care.

PS7-2

Neuro-Epidemiological Research in India – An Overview
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Objective: Over the past few decades, several well-designed neuro-epidemiological studies have been carried out from different parts of India. The aim of this article is to present the data from various studies and critically analyze the methodologies adopted. Besides, the Indian data are compared with that of other developing and developed countries.

Methods: We collected data from the population-based studies from both rural and urban India and also from the hospital based studies on the following neurological disorders: Epilepsy, Stroke, Parkinson’s disease and Dementia. We searched all relevant articles on Medline and particularly in the journals e.g., JAPI, Neurology India and Neurology Asia from 1970 onwards till date.

Results: Prevalence of neurological disorders varies from 967 to 4070 per 100,000 populations. Rural population has greater prevalence than urban population. Overall stroke incidence and prevalence and mortality are higher as compared to developed countries. There is a regional difference in prevalence of neurological disorders such as epilepsy, which is higher in southern parts of India. Out of stroke, hemorrhagic stroke is commoner in eastern and northeastern region of the country. Prevalence and incidence of neurodegenerative diseases such as Parkinson disease and dementia are lower as compared to developed countries. Parsis, a distinct ethnic group has high prevalence of neurological disorders, partly contributed by their high aging population.

Conclusion: Many of the study data lacked age standardization and hence proper comparison of prevalence and incidence rates among different communities could not be done. It is necessary that all future population-based studies from different regions adopt a common well-designed methodology. Besides there is a need for many more prospective studies to determine the incidence, mortality and fatality rates of various major neurological disorders considering multiethnicity of Indian population.

PS7-3

Pharmacotherapy of Epilepsy: A ‘Voice Chat’ Between – Ion Channels, Neurotransmitters and Anti-Epileptic Drugs
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Epilepsy a common, complex and chronic neurologic disorder affects an estimated 0.5–1% of the global population. Antiepileptic drugs [AEDs] as pharmacologic agents are considered the mainstay in the treatment of epilepsy with an ultimate goal to eliminate seizures without producing many side effects. Effective control of epilepsy is often possible with use of single AED, however episodes persist among 30 and 50% of patients despite increasing dosages with monotherapy and use of polytherapy. While, drug’s efficacy is important, equally important are tolerability and safety profile. Bromide the first AED introduced for use in epilepsy was a failure due to its serious adverse effects. A large number of AEDs have been introduced over the last two decades. An ideal AED is yet to be designed and hence current research is focused on identifying AED having specific action on neuronal receptors to avoid unwanted effects. Exploring the mechanism of action of AEDs therefore play an important role to explain reason for adverse events experienced by patients. It is suggested that ‘isobolographic’ analysis an experimental technique is considered as a valuable tool that allows precise classification of exact types of interactions between AEDs and has been successful in animal models. It allows systematic approach to predicting pharmacologic actions of given combination and is hence proposed to identify potential adverse reactions of AEDs. Recently the use of AED combinations is a common practice. Hence the need to evaluate drug-drug interactions to understand influence of these on safety, economic burden, quality of life in addition to efficacy becomes important. In this regard designing ‘rational’ therapeutic regimens by clinicians is necessary where the mechanisms of action play a major role and knowledge of pharmacology of receptors, ion channels and neurotransmitters are essential. Such analysis is said to allow for a more systematic and rational approach to predicting whether a given combination of AEDs will result in a greater or lesser pharmacologic effect. With this background understanding the mechanisms of actions of AEDs to improve clinical outcomes in patients with epilepsy for improved medication acceptability, achieve seizure freedom with optimal quality of life should be the goal. While, newer AED combinations are currently administered empirically as add on therapies in routine practice, these have not been evaluated for compatibility. We have been successful in identifying antagonistic drug interactions at adenosine receptor sites through limited numbers of experimental studies in various ani-
PS8 – Selected Aspects of Neuroepidemiology of Stroke and Epilepsy – 4

PS8-2
Effects of Early Blood Pressure Lowering on Outcome After Acute Stroke

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Hypertension is common in the setting of acute stroke. The effects of acute blood pressure lowering on stroke outcome is controversial. We sought to review the effects of acute blood pressure lowering after stroke and stroke outcome through a literature search. Pooled results showed that early BP lowering had no significant effect on early deterioration, long term death, and long term dependency.

PS8-3
Overview of Stroke Epidemiology in Children

Mackay M.
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Childhood stroke is considered to be rare by adult standards but ischemic and hemorrhagic strokes are collectively more common than brain tumors. Stroke etiologies differ substantially from adults. Non-atherosclerotic arteriopathies and cardiac disorders are the most commonly identified causes of ischemic stroke. Arteriovenous malformations are the most commonly identified cause of hemorrhagic stroke. Many disorders are reported to be risk factors for childhood stroke but causal relationship is often unproven due to lack of evidence from case controlled studies. However it is becoming increasingly clear that infection, particularly the herpes viruses, are important risk factors for childhood ischemic stroke. Age and geographical variations in risk factors will be explored and the influence of etiology on mode of presentation and infarct topography will be discussed. The importance of a comprehensive diagnostic work up, particularly vascular imaging will be highlighted. Current international collaborative research initiatives including multicenter registries and development of stroke classification systems will also be discussed.

PS7-4
Limitations of Conventional Rehabilitation for Stroke

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Stroke is a serious condition that negatively affects patients and their families. Up to 85% of stroke patients experience weakness in their arms and legs immediately after a stroke. Approximately two out of three stroke survivors continue to experience some level of disability in performing daily activities. Conventional rehabilitation (i.e. physiotherapy, occupational therapy) involves methods to improve motor function or to restore body movements back to normal. However, the techniques used in usual rehabilitation programs can be tedious, costly, usually requiring transportation of stroke patients to special rehabilitation centers (Table 1). Hence, new rehabilitation techniques (e.g. virtual reality, robotics) are emerging to improve the life of stroke survivors. The entertainment industry has developed a new and possibly useful technology that can be used in rehabilitation: virtual reality (VR) games. Virtual reality games allow a person to experience and handle life-like situations, which have been created by a computer system. This technology (i.e. Nintendo Wii®, Kinect, Playstation, among other devices) is less costly, widely available, and could be used in patients’ homes. In addition, this technology uses important concepts in rehabilitation, and may improve arm and/or leg movement after a stroke. A pooled analysis of 5 small randomized trials revealed that patients assigned to virtual reality had nearly 5-fold higher likelihood of achieving a motor improvement (OR = 4.89; 95% CI, 1.31 to 18.3). It is expected that in the next 2–3 years, the results of larger randomized clinical trials using VR would provide answers on how to best utilize new promising therapeutic opportunities for stroke recovery. For example, EVREST Multicenter (which follows EVREST Pilot) was designed with the hypothesis that VR may provide an affordable, enjoyable and effective alternative to intensified treatment and promote motor recovery after stroke (http://clinicaltrials.gov/show/NCT01406912). The use of a novel, simple, wireless, and widely available 3D virtual reality technologies may allow the implementation of proven concepts in stroke rehabilitation (repetitive, high-intensity and task-specific activities) to improve motor function even for home use. The results of the ongoing RCTs will advance knowledge about the optimal rehabilitation strategy for patients with a disabling stroke. In this presentation, we will be reviewing recent advances using virtual reality technology in stroke rehabilitation.
PS10 – Global and Regional Burden of Stroke and ALS – 2

PS10-1
Global and Regional Stroke Burden Overview
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Despite decreasing stroke mortality worldwide, stroke burden in terms of absolute number of people affected by stroke, stroke survivors, and disability-adjusted life years (DALY) lost is increasing. This presentation will highlight the main results of the Global Burden of Disease (GBD) 2010 Study relevant to global and regional stroke burden. In particular, it will be demonstrated that from 1990 to 2010 there was a statistically significant 12% (95% CI 6%, 17%) decrease in age-standardised stroke incidence rates in high-income countries (HIC), and a 12%, albeit not statistically significant (95% CI –3%, 22%), increase in stroke incidence rates in low and medium income countries (LMIC). There was a statistically significant decrease in age-standardised stroke mortality rates in both HIC (37%; 95% CI 31%, 41%) and LMIC (20%; 95% CI 15%, 30%). In 2010, the absolute number of people with first stroke (16.9 million), stroke survivors (33 million), stroke related deaths (5.9 million) and DALYs lost (102 million) were high and had significantly increased since 1990 (40%, 46%, 20% and 16% increase respectively), with the bulk of the burden (68.6% incident strokes, 52.2% prevalent strokes, 70.9% deaths from stroke and 77.7% stroke related DALYs lost) currently borne by LMIC. In 2010, 5.2 million of strokes (31%) happened in children (<20 years old) and young/middle-age adults (20–64 years), of which children and young/middle-age adults of LMIC constituted almost 74,000 (89%) and 4.0 million (78%), respectively. There are also significant (3–10 fold) geographical differences in stroke burden among GBD regions and among countries. Over 62% of new strokes (50% in HIC and 68% in LMIC), 69.8% prevalent strokes (60.5% in HIC and 78.3% in LMIC), 45.5% of deaths from stroke (27.4% in HIC and 52.8% in LMIC), and 71.7% DALYs lost due to stroke (53.8% in HIC and 76.8% in LMIC) occurred in people under 75 years of age.

PS10-3
Overview of Stroke Epidemiology in Developing Countries
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MD DM FRACP – Professor and Head, Department of Neurology – Deputy Director, Research and Development – Christian Medical College, Ludhiana, Punjab, India

Based on the recent Global burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) the age-standardised incidence of stroke has decreased by 12% in developed countries and has increased by 12% in developing countries. The age adjusted incidence rate in low to middle income countries (LMICs) is 281.12/100,000 and in high income countries (HICs) is 217.26/100,000. There is lack of good quality stroke epidemiological information available from developing countries. Stroke incidence studies have been reported from Nigeria, Tanzania, Brazil, Chile and India (Trivandrum, Kolkata, Mumbai, Ludhiana). Researchers have used door-to-door survey and also WHO STEPS methodology to ascertain the first ever stroke cases in the community. The annual incidence rate per 100,000 in LMICs is from 25.2 to 145 and the case fatality rate (CFR) is 16 to 41%. The annual incidence rate in Ludhiana city is 140/100,000 and CFR is 22% based on the recently concluded population based stroke registry. This project was supported by the Indian Council of Medical Research (ICMR) under the Task Force Scheme. The feasibility phase of this project revealed many practical problems in carrying out this study. Locally applicable solutions were implemented in documentation of deaths and in collection of data from general practitioners and scan centres. There is a need for good quality epidemiological studies from developing countries.

PS10-4
Updates on Stroke Epidemiology in Japan
Kokubo Y.
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Stroke mortality is the fourth leading cause of death in Japanese men and women, although it has been drastically decreasing. Age-adjusted (the Japanese model population in 1985) mortality rates of stroke, cerebral infarction, intracerebral infarction, and subarachnoid hemorrhage were 285.3, 8.9, 266.7, and 2.9 in men and 229.4, 7.1, 213.9, and 2.9 in women, respectively, per 100,000 population in 1951. Then those of stroke (in 1965), cerebral infarction (in 1970), and subarachnoid hemorrhage (in 1995) subsequently increasing to 361.0, 115.5, and 7.9 in men and 243.8, 77.1, and 9.6 in women, respectively. Since then, they drastically decreased to 42.0, 21.0, and 4.9 in men and 23.3, 10.8, and 4.9 in women, respectively in 2013. Meanwhile, intracerebral infarction mortality rates have consistently decreased (15.0 in men and 6.9 in women in 2013). One of the longest population cohort study in Japan, named the Hisayama study, has shown that age-adjusted incidence rate of cerebral infarction, intracerebral hemorrhage, and subarachnoid
hemorrhage were 950, 375, and 70 in men and 531, 78, and 84 per 100,000 population in 1961–1968, and were decreasing to 270, 104, 41 in men and 145, 35, and 32 in women in 2002–2009, respectively. The study has also shown that the age-adjusted incidence of cerebral infarction, lacunar infarction declined significantly. However, the incidences of atherosclerosis and cardioembolic infarction have not changed since 1961. Intracerebral hemorrhage incidence steeply declined from the 1960s to 1970s, but afterward the decline has attenuated, probably because of increased incident thalamic hemorrhage in the elderly in recent years. For cardiovascular risk factors, blood pressure control improved significantly and the smoking rate decreased, but the prevalence of diabetes, dyslipidemia, and overweight or more increased steeply. Small- to medium-sized HDL cholesterol levels were inversely associated with incident stroke and its subtypes. The high-normal blood pressure subjects in all glucose categories and the normal blood pressure subjects with impaired fasting glucose showed increased risk of stroke in the Japanese population. Among the Japanese traditional food, fish and soy products have most protective effects of cardiovascular disease. An inverse association between fish and omega-3 PUFA dietary intakes and cardiovascular disease mortality in Japanese population. High isoflavone intake was associated with reduced risk of cerebral infarction in Japanese women. The risk reduction was pronounced for postmenopausal women. Rice, which is one of the main Japanese staple food, is not associated with risk of CVD morbidity or mortality, although some of previous cohort studies have shown that rice consumption was associated with risk of type 2 diabetes. Higher green tea and coffee consumption were inversely associated with risk of stroke in the Japanese population. Higher total dietary fiber was associated with reduced risk of cerebral infarction in the elderly. The study has also shown that rice consumption was associated with reduced risk of cerebral infarction in Japanese women. The age-adjusted incidence of cerebral infarction, lacunar infarction declined significantly.

### PS11 – Global and Regional Burden of Stroke and ALS – 3

#### PS11-1

**New Therapeutic Strategies to Reduce Cerebrovascular Permeability After Neurotrauma**

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The blood-brain barrier (BBB) is a highly regulated interface between the circulation and the CNS that is commonly disrupted following traumatic brain injury (TBI) and can lead to cerebral oedema with devastating consequences. We have studied changes in BBB permeability in mice subjected to neurotrauma using the controlled cortical impact model of TBI. Our investigations revealed an important role for the plasminogen activating (PA) and matrix metalloproteinase (MMP) group of proteases that work in concert to promote BBB opening following TBI. We observed that cerebral extravasation was substantially reduced in t-PA deficient (t-PA/-/-) mice within 3 h following TBI, whereas greater extravasation and neurological impairment was seen in transgenic mice selectively overexpressing t-PA in neurons (‘T4 mice’); hence t-PA causes a dose-dependent increase in BBB permeability. We also observed a concomitant increase in the MMPs in the ipsilateral cortex of mice following TBI. This increase in MMPs is also likely to further increase BBB permeability via direct proteolysis of the basal lamina of the neurovascular unit. We reasoned that inhibition of t-PA would be of benefit in the host response to TBI. t-PA is naturally inhibited by plasminogen activator inhibitor 1 (PAI-1), neopterin (NS) or protease nexin-1 (PN-1) by the formation of inhibitor:protease complexes that are cleared via low density lipoprotein receptors (LDLRs). Surprisingly, inhibition of t-PA activity following direct intracortical administration of PAI-1 into the lesioned brain after TBI increased BBB damage despite reducing endogenous t-PA activity by more than 90%. This paradoxical finding was due to the formation of t-PA:PAI-1 complexes in the brain parenchyma that bound to LDLRs most likely on astrocytes that initiated extracellular signalling across the plasma membrane that in turn triggered the recruitment of the MMPs. Inhibition of the binding of t-PA:PAI-1 complexes to LDLRs using a specific LDLR receptor antagonist, or administration of specific MMP inhibitors significantly reduced cerebral extravasation 3 h post-TBI. Hence, t-PA can increase BBB permeability indirectly via inhibitor:protease complex formation and downstream activation of LDL receptor signalling and MMP recruitment. Concentrations of both t-PA:PAI-1 complex and MMP-3 were also shown to be elevated in cerebrospinal fluid of TBI patients and furthermore correlated with neurological outcome. Collectively, these findings support the concept that MMP inhibition together with blockade of LDLRs could be an effective means to reduce cerebral extravasation following TBI.

### PS11-4

**Tranexamic Acid for Spontaneous Intracerebral Hemorrhage; Review of Literature and Trial Protocol**

**STOP-AUST**

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Spontaneous intracerebral hemorrhage (ICH) can cause significant mortality and morbidity with hematoma expansion (HE). Tranexamic acid (TA), an antifibrinolytic drug, significantly reduced mortality in bleeding patients after trauma in CRASH-2 trail. The CRASH-2 ICH substudy suggested that TA reduced mortality and dependency in traumatic ICH (nonsignificantly). At present, there is evidence based therapies for ICH. This paper discuss the trial potential role of TA on preventing ICH growth in the context of STOP-AUST trial protocol.
SS1 – Neurological Consequences of Global Change

SS1-1
The Boomerang Effect: Health Risks [for the Brain] from Global Change
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Knowledge of the anthropogenic modification of the environment is constantly improving. Nowadays, the impact is obvious and a no-return point may have been reached. Thus a new word 'Anthropocene' has been coined by Paul CRUTZEN in 2000 to designate a new geological era. This new era is also characterized by the boomerang effect: the health consequences for Man of all the global changes he is inducing. When reviewing the global changes from a focused point of view, looking precisely on neurological consequences, three main themes arise: climate change illustrated by the global warming and extreme weather, air pollution with greenhouse gases emission and diffuse chemical pollution. The impact on human health of climate, weather and seasonality has been recognized since Antiquity (Hippocrates). Two facts are recent: first, detailed analysis of the complex and multifactorial effects of global changes on health; second the progressive awareness that these global changes can affect human health by a feed-back process. Human activity has modified the environment in a heterogeneous way. Environmental stressors result from diverse mechanisms, including fossil energy combustion, increasing release of human-produced greenhouse gases altering the climate system, and non-controlled usage of chemical compounds. The consequences are environmental alterations that directly or indirectly impact human health. The third part of our review seeks to untangle the complex interactions that lead to neurological consequences for a better targeting of prevention and precaution. Four examples demonstrate the impact of climate change on the human nervous system: Central nervous infections, stroke, neurodegenerative diseases, and developmental brain toxicity.

SS1-2
Climate-Sensitive Toxins in Food Linked to Neurological Disease
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Objective: To describe how climate change, notably global warming, impacts human exposure to naturally occurring chemicals in bacteria, fungi, plants and animals that cause human and veterinary diseases of the nervous system.

Methods: Field, epidemiological and laboratory research on neglected neurological diseases, including amyotrophic lateral sclerosis and parkinsonism-dementia complex (ALS-PDC), lathyrism, cassavism, seafood toxicity, and Nodding Syndrome.

Results: Geographic isolates of high-incidence, non-infective neurological disease occur in populations subject to specific environmental exposures, most commonly from the use of food containing natural neurotoxins. (a) Temperature-sensitive harmful algal blooms elaborate potent neurotoxins that bioaccumulate in seafood and trigger profound neurophysiological dysfunction after ingestion. Ciguatera is a globally widespread neurological illness caused by eating fish contaminated with ciguatoxin and maftoxin, neurotoxic biotoxins synthesized by the dinoflagellate Gambierdiscus toxicus. Endemic to tropical and sub-tropical regions of the Pacific Basin, Indian Ocean and Caribbean, ciguatera is seen with increasing frequency in temperate areas, such as Europe and North America, where coastal algal blooms have increased in part from rising water temperatures. Other neurological illnesses resulting from ingestion of biotoxin-contaminated seafood include Paralytic Shellfish Poisoning (saxitoxin) and Amnesic Shellfish Poisoning (domoic acid). (b) Food-related neurological and neurodegenerative disorders are linked to dietary dependency on environmentally tolerant plants that resist drought, flooding and high winds that destroy other food crops. Corticospinal degeneration resulting in persistent spastic paraparesis is the outcome of dietary dependence on the grasspea (Lathyrus sativus), a protein-rich legume that has caused lathyrism in Asia, Africa, Europe and South America. Food dependency on cassava, a protein-poor, drought-resistant tuber that is widely eaten in the tropics and sub-tropics, continues to cause outbreaks of spastic paraparesis (cassavism) in certain food-insecure African populations. Food prepared from cycads, an environmentally hardy species that causes neuromuscular disease in grazing animals, is epidemiologically linked with ALS-PDC in Guam. (c) Other food-related causes of neurological disease in humans and animals include tremorgenic and other mycotoxins that contaminate food plants under certain weather conditions. Best known are the European and Russian outbreaks of convulsive ergotism in the Middle Ages; these were caused by eating bread containing the fungus Claviceps purpurea. Food contamination with mycotoxins is a major health hazard globally, especially among impoverished populations in Africa. The subject has attracted research attention in relation to Nodding Syndrome (research supported by NS079276), an idiopathic developmental and seizure disorder of children, epidemics of which since the 1990s have impacted food-insecure populations of South Sudan and Uganda.

Conclusions: Climate change, which appears to be resulting in the northerly and southerly expansion of warm temperatures, is predicted to impact the geographic distribution of bacterial, fungal, plant and animal species that produce or contain substances with human neurotoxic potential. Populations subject to food shortages, including those associated with weather extremes, will continue to rely on environmentally tolerant plants with the potential to cause neurological disease. The culpable neurotoxins are not only causes of neurological disease but also valuable agents to probe nervous system vulnerability and the pathogenesis of a wide range of CNS and PNS disorders.
**Session O1. Prevention**

**633**

**An Analysis of Cognitive Processes Associated with Nurses’ Day and Night Shifts**

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**Objective:** Nursing involves high cognitive load that are associated with nurses’ thought processes to ensure proper medication administration. Stress-related disorders (SRDs) commonly affect nurses possibly due to the strenuous workload and irregular work shifts that are an integral part of this emotionally demanding job. The purpose of the present study is to analyse the cognitive processes associated with nurses at work between day and night shifts.

**Methods:** Participants consisted of twenty-six registered nurses (14 females and 12 males) from government and private hospitals of similar size. All participants worked in full-time basis and were matched by terms of age, education, and marital status. They worked in cardiothoracic unit (n = 6), in neurosurgery unit (n = 6), in intensive care unit (n = 6), in trauma and casualty (n = 4), in gynaecology unit (n = 4). For each participant measurements were taken twice, with one day shift and one night shift. The order in which the participants worked at shifts was randomized. Subjective sleepiness was assessed by means of Stanford Sleepiness Scale, a 7-point self rating scale from one (feeling active) to seven (no longer fighting sleep), every hour during day and night shifts when working. Participants were also asked to perform cognitive task, requiring the ability to solve arithmetic and logical operations, and maintain an appropriate puzzle-solving strategy. Each task was performed four times during the shift. To obtain an objective measurement, the electroencephalogram (EEG) was recorded within a regular interval of time during day and night shifts.

**Results:** Self-rated sleepiness was significantly (p < 0.005) higher during the night shift than during the day shift. During the night shift there was an increase in sleepiness across time, whereas sleepiness during the day shift showed a tendency, with levels falling initially and rising again towards the course of the shift. The study also reveals that sleepiness decreased immediately between pre- and post-break and then slowly increased again. The number of errors, that is, deviations from the ideal strategy of cognitive task did not differ between shifts. There was, however, a tendency for the number of errors to be higher during the night shift. It has been observed from the EEG analysis that mean value of relative wavelet packet energy in beta frequency band on frontal, parietal and occipital lobes significantly decreased (p < 0.05), while mean value of alpha and theta frequency bands on frontal and occipital electrodes significantly increased (p < 0.05) between day and night shifts.

**Conclusion:** The present study investigated that nurses’ night shift work is associated with high sleepiness and limits the capabilities of cognitive processes. This might be caused due to circadian rhythm disruption. Therefore, this result should be incorporated in the discussions on the promotion of nurses’ health and patient safety in relation to changes in the nursing work system.

**649**

**Effect of Yoga Practice on Stress Reduction Among Gen Y School Children**

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**Objective:** Stress is one of the serious problems in daily lives especially for Generation Y teenagers. This is considered as the most important risk factors for suicide. Generation Y – also called Gen Y is defined by the term ‘Digital Native’ – internet and an increasingly globally connected world. According to the world health organization (WHO), stress is estimated to become the second leading causes of dysfunction by the year 2020. Higher levels of stress for Gen Y school children may have a negative impact on their learning ability that affects the student academic achievement and may also lead to psychological and physical problems. Yoga practice is reported to lead to reduce stress-related symptoms such as frustration, conflict, and anxiety and thus improve the psychological functioning. The present study was carried out with an objective to assess the effect of yoga through mindfulness training on stress reduction among Gen Y school children.

**Methods:** The study was conducted in ten public schools of south region of India. Gen Y school children with age group of 14–15 years participated in this study. Bisht Battery of Stress Scale (BBSS) was administered on 400 students (Male: Female = 133:87).
with 220 of experimental group (students practicing yoga through mindfulness training) and 180 (M:F = 133:47) of control group (students not practicing yoga). The BBSS was administered to categorize two stress levels of the school children, i.e., high stress (150) and low stress (142). This test was framed to quantify 13 types of stress. Two scales, i.e., scale of academic stress and scale of achievement stress were selected out of 13 scales. These scales were included of 52 and 80 items, respectively, which were 132 in total.

**Results:** The parametric unpaired t-tests were performed, which indicates that Gen Y school children of experimental group and the control group were significantly (p < 0.05) differ on the total score, academic stress and scale of achievement stress. Compared to control group, yoga practitioners demonstrated significantly less stress score. Yoga group reported less frustration, conflict, and anxiety as compared to the non-yoga group. It was also seen that stress was significantly more among the males than the females, regardless of the groups.

**Conclusion:** With yoga through mindfulness training the stress-related symptoms was controlled indicating the benefits of yoga in cognition and academic achievement. The present findings suggests that yoga through mindfulness training can reduce perceived stress, and a substantial improvement in psychological well-being of Gen Y school children.

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**672**

**Altered Levels of IL-27 in The Cerebrospinal Fluid and Plasma of Patients with Guillain-Barré Syndrome**

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**Objectives:** Guillain-Barré syndrome (GBS) is an immune-mediated disorder in the peripheral nervous system. In previous investigation, numerous immune factors are found play an important role in the pathogenesis and/or the development of GBS. A lower concentration of IL-27, an anti-inflammatory cytokine, is observed in several autoimmune diseases. However, the IL-27 level in cerebrospinal fluid (CSF) and plasma of GBS patient has not been studied in GBS. Our research aims to have a comparable study on the altered level of IL-27 between GBS and other nervous system diseases and to explore the correlation between the level of IL-27 and the clinical manifestations of GBS patients.

**Methods:** Enzyme-linked immunosorbent assay (ELISA) was used to measure the concentrations of IL-27 in paired samples of CSF and plasma from 31 patients with GBS and 7 with encephalitis or meningitis (group 1), 5 controls with spinal cord disease (group 2) as well as 11 patients with other non-inflammatory neurological disorders (group 3). The correlation between the level of IL-27 and manifestation of GBS patients was analyzed by SPSS 18.0.

**Results:** The mean of IL-27 concentration in CSF of GBS patients (194 pg/ml) was lower than the other controls (group 1, 269 pg/ml; group 2, 281 pg/ml; group 3, 244 pg/ml) (p < 0.05). As in plasma, the mean concentration was 237 pg/ml for GBS patients and 307 pg/ml, 247 pg/ml, 313 pg/ml for group 1 to 3 respectively. The IL-27 levels in CSF of the GBS patients with cranial involvement, decreased reflexes, hypesthesia, autonomic nerve dysfunction, MRC score <30 were lower than the levels of GBS patients without those symptoms (182 pg/ml, 181 pg/ml, 185 pg/ml, 195 pg/ml, 194 pg/ml vs 211 pg/ml, 205 pg/ml, 202 pg/ml, 198 pg/ml, 199 pg/ml). Similar results appeared in plasma except cranial involvement as well (196 pg/ml, 220 pg/ml, 233 pg/ml, 235 pg/ml vs 273 pg/ml, 252 pg/ml, 241 pg/ml, 247 pg/ml).

**Conclusions:** Our data provides preliminary evidence that GBS is associated with lower CSF and plasma levels of IL-27 than other nervous system diseases. And more severe manifestation tends to relate to a lower level of IL-27. We speculate that IL-27 has a particular anti-inflammatory function in GBS. Further studies are needed to identify the underlying mechanisms behind IL-27 alterations.

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**673**

**More Severe Manifestations and Poorer Short-Term Prognosis of Ganglioside-Associated Guillain-Barré Syndrome in Northeast China**

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Ganglioside as a neurotrophic drug has been hitherto widely used in China, although Guillain-Barré syndrome (GBS) following intravenous ganglioside treatment was reported in Europe several decades ago. We identified 7 patients who developed GBS after intravenous use of gangliosides (ganglioside+ group) and compared their clinical data with those of 77 non-ganglioside-associated GBS patients (ganglioside-group) in 2013, aiming at gaining the distinct features of ganglioside-associated GBS. Although the mean age, protein levels in cerebrospinal fluid (CSF) and frequency of cranial nerve involvement were similar between the two groups, the Hughes Functional Grading Scale (HFGS) score and the Medical Research Council (MRC) sum score at nadir significantly differed (4.9 ± 0.4 vs 3.6 ± 1.0; 7.7 ± 5.5 vs 36.9 ± 14.5, both p < 0.001), indicating a higher disease severity of ganglioside-associated GBS. A significant higher ratio of patients with ganglioside-associated GBS required mechanical ventilation (85.7% vs 15.6%, p < 0.01). The short-term prognosis of ganglioside-associated GBS, as measured by the HFGS score and the MRC sum score at discharge, was poorer (4.3 ± 0.5 vs 2.8 ± 1.1; 17.3 ± 12.9 vs 46.0 ± 13.9, both p < 0.001). All the patients in the ganglioside+ group presented an axonal form of GBS, namely acute motor axonal neuropathy (AMAN). When compared with the AMAN patients in the ganglioside-group, more severe functional deficits at nadir and poorer recovery after standard treatment were still prominent in ganglioside-associated GBS. Anti-GM1 and anti-GT1a antibodies were detectable in patients...
with AMAN while not in patients with the demyelinating subtype of GBS. The concentrations of these antibodies in patients with AMAN were insignificantly different between the ganglioside+ and ganglioside-groups. In sum, ganglioside-associated GBS may be a devastating side effect of intravenous use of ganglioside, which usually manifests a more severe clinical course and poorer outcome.

Current methods of assessing and modifying stroke risk are difficult to access and implement by the general population, amongst whom most future strokes will arise. To help reduce the burden of stroke on individuals and the population a new app, the Stroke Riskometer™, has been developed by the National Institute for Stroke and Applied Neurosciences, AUT University (Auckland, New Zealand). This app utilizes recent advances in risk presentation/communication, international guidelines on stroke and CVD prevention and has the potential to significantly improve stroke and other major non-communicable disease prevention (e.g. ischemic heart disease, dementia and diabetes). The Stroke Riskometer™ algorithm was derived from the Framingham Stroke Risk Score (FSRS) prediction algorithm and enhanced to improve accessibility and to include several additional major risk factors shown to be important for stroke, largely based on the INTERSTROKE study. Endorsed by the World Stroke Organization, World Federation of Neurology and International Association on Neurology and Epidemiology, the app provides estimates of the absolute risk of stroke within the next 5 and 10 years for individuals aged ≥20 years. Importantly, the Stroke Riskometer™ provides not only their absolute risk of stroke development but also a baseline risk for comparison, thus allowing users to compare their risk of stroke with someone of the same age and gender who has no risk factors. The former represents a new paradigm for high-risk stroke prevention strategy, and enables a refined presentation of the traditional threshold-based approach in which people are categorized into low, moderate, and high-risk groups. This procedure enables not only those at high levels of risk, but also those at low- to moderate absolute risk, to reduce their risk of stroke. The app therefore allows a combination of both high-risk and population strategies, an approach shown to be the most effective for cardiovascular disease prevention.

**Session O2. Diagnosis**

### 628

**An EEG Investigation on Critical Thinking Between Men and Women**

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**Objective:** Critical thinking is a metacognitive process that promotes an individual's problem-solving ability and logical decision-making in real-world applications. Critical thinking skills are needed to help individuals better able to cope with the rapidly evolving technological society. The manner in which men and women conceive a problem and give the solution to that problem is quite different. The objective of this study is to investigate the differences in electroencephalographic (EEG) activity between men and women in critical thinking.

**Methods:** Twenty right-handed technical university students (10 males and 10 females, aged 16–20 years) voluntarily participated in this study. Participants were chosen by the intelligent pregnancy (using Amthauer's Intelligence Scale) that were measured two weeks before the commencement of this study. EEG was recorded during a 10 minutes resting period and a performance of the critical thinking task with closed eyes. Five conventional scalp sites of the 10–20 electrode placement system were used: frontal, parietal, central, temporal and occipital leads (Fp1, Fp2, F3, F4, P3, P4, C3, C4, T3, T4, O1, and O2, correspondingly). Wavelet packet decomposition analysis was performed with artifact free EEG epochs of 20 seconds of data for every 2 minutes while resting and while solving problems during critical thinking. Relative wavelet packet energy indices were calculated in each of the four frequency bands in the 0.4–30 Hz range (delta, 0.4–4 Hz; theta, 4–7 Hz; alpha, 8–12 Hz; beta, 13–30 Hz).

**Results:** EEG investigation suggests that there are distinct differences between men and women with regard to their problem solving ability with critical thinking. Gender differences in EEG data were obtained only in the alpha and beta bands. Men were characterized by massive increases of beta activity whereas women showed more local increases of the beta activity. There was a significant (p < 0.05) increase of beta activity on frontal, parietal and temporal lobes in men as compared to women. Alpha activity in women was more expanded as compared with men.

**Conclusion:** The data reported here deal with only the frequency of the dominant rhythm of EEG and analyzed the gender differences in critical thinking. Thus, the demonstrated differential associations of alpha and beta activity with problem solving tasks in men and women may show an existence of gender differences in critical thinking processes.
Toxic leukoencephalopathy is usually a structural alteration of white matter of the brain secondary to various agents, without special clinical manifestations but usually has a typical radiologic image. Morantel is an anthelmintic used for prevention and control of ostertagiasis. It mainly targets at adult worms and developing larvae with low toxicity and has been widely used for all classes of cattle including lactating dairy cattle at any stage of lactation. So far, there has been no report on morantel-induced toxic leukoencephalopathy. Morantel was further detected in the blood of the patient. Diagnosis of morantel-induced toxic leukoencephalopathy was thus established. Treatment with corticosteroid resulted in a complete resolution of the clinical symptoms and the MRI anomalies.

**Session 03. Epidemiology**

**594 Stroke Predictors in the Early 60s: The Path Through Life Project**

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**Objectives:** The identification of population-specific stroke predictors is essential to the implementation of preventative programs in the community. A number of risk factors for stroke have been clearly identified in previous clinical and epidemiological cohort studies. They include hypertension, heart disease, TIA, smoking, diabetes as well as sex, age, race and other, less easily measured factors. Most past investigations have covered broad age ranges, heterogeneous population, and have particularly focused on cardiovascular risk factors. It is therefore not clear whether, in addition to well-established risk factors, other individual characteristics may assist in predicting those at higher risk of stroke, and particularly in the 60s which has been identified as the age window with highest risk. The aim of this study was to investigate longitudinal predictors of incident stroke in a large epidemiological sample of cognitively healthy individuals in their early 60s.

**Methods:** Participants (n = 2551; 60–64 years) from the PATH Through Life Project, a large longitudinal study of ageing, were considered for inclusion in this investigation. After applying exclusion criteria (existing cognitive impairment, prior history of stroke or TIA, neurological disorder, missing or lack of follow-up data) 1774 participants were available for analysis including 28 individuals who experienced a stroke in the subsequent 8 years. Multiple measures in five domains (cardiovascular, lifestyle, mental health, cognition, and personality) were investigated as predictors of stroke. Logistic regression analyses including all selected participants were first conducted. Additional nested case-control analyses were conducted on a selected sub-sample including the 28 individuals with incident stroke and 140 controls (five per case) carefully matched on sex, age, education, race, and height to examine whether findings from the first set of analyses were influenced by the more variable nature of the normative sample.

**Results:** The cohort selected had a mean age of 62.5 years (SD 1.5) and was 48.6% female with an average of 14.1 years of education (SD 2.6). When 28 individuals with incident stroke were compared to the remaining 1746 cognitively healthy individuals the only significant predictors of stroke after controlling for gender, age, and education were systolic blood pressure (per unit above 140 mm Hg: OR 1.04, 95% CI 1.01–1.07, p = 0.002), smoking (trend OR 2.28, 95% CI 0.99–5.24, p = 0.052), and psychomotor skills (OR 0.80, 95% CI 0.62–0.96, p = 0.037). Findings remained largely unchanged when analyses were not controlled for gender, age and education. In matched-control analyses no significant group difference was present for age, education, and height while sex and race were matched exactly indicating that the matching procedure was highly effective. However, significant group differences were found for systolic blood pressure (p = 0.001), smoking (p = 0.036), and psychomotor skills (Purdue Pegboard; p = 0.028).

**Conclusions:** In this cohort of community-dwelling individuals risk of incident stroke in the early 60s was only predicted by higher systolic blood pressure, smoking and psychomotor skills. These results suggest that in generally well-educated individuals strokes are mostly associated with established cardio-vascular risk factors. Of note is that every one unit increase in systolic blood pressure above 140 was associated with a 4% increased risk of stroke.

**644 The Danish Multiple Sclerosis Registries: A Unique Resource for Epidemiological and Clinical Studies**

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Collecting data on patients with multiple sclerosis (MS) has a long tradition in Denmark. Denmark has two MS registries; The Danish Multiple Sclerosis Registry and The Danish Multiple Sclerosis Treatment Register. The Danish Multiple Sclerosis Registry which today has developed into a unique resource was first established in 1956 and comprises all Danish citizens who
Oral Presentations

have received a diagnosis of MS or suspected MS by a neurologist or a neurology department since 1949. Data on new cases are reclassified at entry according to standardized diagnostic criteria and updated information on persons with an MS diagnosis already notified is continuously collected. Cases that do not fulfill the diagnostic criteria are excluded. In Denmark, the departments of neurology in public hospitals play a key role in diagnosing and treating MS. They diagnose close to all MS cases, lumbar puncture is customary as standard procedure, only these departments are authorized to prescribe disease modifying drugs, and relapses are treated with iv. corticosteroids which requires admission. Practising neurologists are the weakest and least reliable source of notification, but they are few and refer virtually all MS patients to the neurology departments. The completeness of The Danish Multiple Sclerosis Registry has been evaluated to about 91% and its validity to about 96%. It currently includes 24,421 patients with a valid MS diagnosis, of whom 13, 532 were alive in December 2012. The registry is the only existing nationwide MS register in the world that covers a period of more than 50 years. The Danish Multiple Sclerosis Treatment Register is an independent unit adjoined to The Danish Multiple Sclerosis Registry for registration of disease modifying therapies. Notification is mandatory and each treatment site enters their data directly into the database. In contrast to The Danish Multiple Sclerosis Registry, The Danish Multiple Sclerosis Treatment Register is a longitudinal registry with follow-up data on relapses, side effects, Expanded Disability Status Scale score, neutralizing antibodies, treatment changes, side effects and social variables. The Danish Multiple Sclerosis Treatment Register currently contains 7,508 cases, and its strength is that notification is nationwide and virtually complete, its weakness that follow-up usually stops when the patient discontinues treatment. In Denmark exceptional conditions exist for registry-based epidemiological research due to: access to high-quality patient registries and demographic databases with a broad range of social, biological and health data and the ability to link data at the individual level by use of the unique Danish personal identification number. This has made the Danish MS registries an effective tool for epidemiological studies. Research based on the MS registries increase the knowledge on the causes, the prevention, and the optimization of quality in the treatment and care of the disease.

Methods: The MS prevalence in different provinces of Iran was delineated from Ettemadifar et al. 2013 and Rezaali et al. 2013. Possible risk factors were derived from the Statistical Yearbook of Iran 1973–1974, comprising totally 15 provinces at that time, with later data on the MS prevalence. The following variables were drawn: population density; climate 1962–1972 (maximum and minimum temperature; rainfall); percentage of urban economically active (EA) in total EA population; production (in mio. Rials) of wheat; barley; pulses; potatoes; onions; sugar beets; cotton; tobacco; oil seeds; aromatic medical herbs; grapes; apples; stone fruits; citrus fruits; pistachios; almonds; dates; tea; the number of slaughtered sheep; goats; cows; and buffaloes; production of pasteurized milk; milk; yoghurt; churned sour milk; ice cream; butter; cheese; number of wage-earners in different industries (total industry; food; textile; wood; paper; chemicals; non-metallic products; basic metal; metal)(all items by population 1974). The presence of manufacturers producing sausages in 1973–1991 was taken from an Internet source. The MS prevalence was dichotomized (0–49 vs. 50+ per 100,000). The non-parametric Mann-Whitney test was used for bivariate associations, and all variables giving a p-value ≤ 0.10 on that step were ranked and entered into multiple linear regression analysis. The final p-value was ≤ 0.05 for statistical significance.

Results: At least borderline significant (p ≤ 0.10) bivariate correlations were found for the following variables: percentage of urban EA among total EA population (p = 0.066); production of sugar beets (p = 0.086); production of aromatic medicinal herbs (p = 0.066); and production of almonds (p = 0.039) (all by population 1974). The presence of a sausage factory in 1973–1991 was also borderline associated with the MS prevalence (p = 0.066). None of the main industry groups was related to MS. In multivariate regression models, including five variables, only the presence of a sausage factory was independently associated with the MS prevalence (p = 0.073 in the standard model; p = 0.007 in the forward inclusion model; and p = 0.005 in the backward elimination model).

Conclusion: The presence of a sausage factory that, according to the literature, may also produce smoked sausages (e.g. hot dogs; ‘Bandari sausages’), showed a strong and independent association with the MS prevalence in 15 former provinces of Iran. This food item which is comparatively new and increasing in Iran’s urban society, should be studied more intensely in future research.

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Multiple Sclerosis Prevalence and the Production of Smoked Sausages in Iran: An Exploratory Ecological Study

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Objectives: In 14 regions, so far, a significant association was found for the production, or consumption, of smoked meat and/or smoked sausages. This correlation was confirmed, so far, in five case-control studies in independent regions. In the present investigation, the association was tested, in bivariate and multivariate ecological analyses, in Iran, with additional consideration of possible climatic and industrial confounders.
Prevalence of Stroke and Associated Risk Factors in Lebanon: Preliminary Data from the Beirut and Mount Lebanon Governorates


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Objectives: Stroke is the second cause of death in the world [1]. During the past four decades, incidence of stroke has declined by over 40% in high-income countries, but has doubled in low- and middle-income countries [2]. As age is one major risk factor for stroke, the ageing of the world population has resulted in increasing stroke prevalence [3]. In the Eastern Mediterranean Region, the combination of rapid population ageing and high prevalence of metabolic syndrome and cardiovascular diseases put this population at high risk for stroke. The aim of this pilot study is to estimate the preliminary prevalence of stroke and associated risk factors among the older Lebanese population living in Beirut and Mount Lebanon governorates.

Methods: The study is part of a pilot study to generate preliminary data on dementia prevalence and associated risk factors in Lebanon. A random sample of 508 participants older than 65 years from Beirut governorate and two districts of Mount Lebanon governorate (Shouf and Aley) were recruited through multi-stage cluster sampling. The research workers door-knobbed the houses and interviewed any person who was 65 years old and above. Dementia was diagnosed though the extensively validated 10/66 Dementia Research Group (DRG) diagnostic assessment [4]. In addition, risk factor questionnaires were administered to the participants. Blood pressure and body mass index (BMI) were also measured.

Results: 508 participants were assessed and interviewed. We excluded 53 participants (13 with missing data and 37 with dementia diagnosed by the 10/66 DRG diagnostic assessment) and analyzed the data for the remaining 455 participants. The mean age was 72.6 (SD 7.3). The crude prevalence of stroke and of transient ischemic attack (TIA) was found to be 5.3% and 2.9%, respectively. The self-reported crude prevalence of hypertension (BMI >30 mm Hg) was 45.1%. Although 98.2% of participants with self-reported hypertension were on antihypertensive medications, only 71.0% of the participants had at least one risk factor for stroke (obesity, undetected hypertension or untreated hypertension on medication, diabetes, heart disease, and TIA).

Conclusions: The preliminary data from this pilot study showed that prevalence of stroke in Lebanon is comparable to that in the Western world. The prevalence of risk factors for stroke is very high among the older population in Lebanon.

References

Catamenial Epilepsy – Uncommon or Underrecognised? A Study on Prevalence of Catamenial Epilepsy Among Women with Refractory Epilepsy

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Introduction: Catamenial epilepsy is a unique epileptic entity characterised by the seizure clusters occurring around certain phases of menstrual. Catamenial epilepsy has been observed in 10%–70% of epileptic women with recurrent exacerbations. There is a wide variation in prevalence of catamenial epilepsy as reported by many studies due to self-observed reports, seizure-menstrual cycle diaries of women with pharmacoresistant and refractory epilepsy. This entity is yet to be recognised with prompt attention and awareness as there is no definite or globally accepted criteria for its precise diagnosis.

Objectives: 1. To assess the prevalence of catamenial epilepsy among women attending epilepsy clinic of our institution. 2. To classify the women with catamenial epilepsy according to the phase of menstrual cycle in which the seizure clusters occur. 3. To analyse the seizure dispersion during menstrual cycle in women with recurrent epilepsy.

Methods: 100 women of age group 15 to 50 years attending the epilepsy clinic of Government general hospital of Chennai in India, with recurrent seizures and on more than one primary anticonvulsant were enrolled and asked to maintain a diary of menstrual cycle, noting down the first day, last day of the menstrual period and to note the date and time of seizures. The clusters of seizure occurrence in relation to the phases of menstrual cycle documented. On the midluteal phase (day 21) of the menstrual cycle, Serum estradiol and progesterone levels were done in women with catamenial epilepsy done and compared with that of their age matched non-catamenial epileptic women. With the results, the prevalence of catamenial epilepsy among the women with recurrent seizures in the reproductive age group will be identified and they are categorised into subtypes of catamenial epilepsy.

Results: 1) Catamenial epilepsy was observed in 20% of women with recurrent and refractory seizures. 2) The catamenial epilepsy was commonly found in the age group of 15 to 25 years in our...
study. 3) The perimenstrual type (C1) was the commonest among the women with catamenial epilepsy. 4) There was statistically significant (p < 0.001) increase in the level of serum estradiol level and decrease in the level of progesterone among women with catamenial epilepsy compared to noncatamenial group. 5) Majority of women with C1 and C2 types of catamenial epilepsy in our study had generalised tonic clonic seizures.

**Conclusion:** Catamenial epilepsy is still an underrecognised entity in India. A significant group of women of reproductive age group have recurrent and refractory seizures on many anticonvulsant polytherapy. There are very few studies analysing the prevalence of catamenial epilepsy in our country. Among the women with pharmacoresistant epilepsy, about one fifth women according to our study fall under the category of catamenial epilepsy. The burden of epilepsy in these women would be reduced with a small step of prompt recognition and appropriate treatment, thus causing a leap in their quality of life.

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**Fig. 1.** For Abstract No. 689.

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**Development of the Standards of Reporting of Neurological Disorders (STROND) checklist: A Guideline for the Reporting of Incidence and Prevalence Studies in Neuroepidemiology**

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**Background:** Incidence and prevalence studies of neurological disorders can play an important role in assessing the burden of disease. However, the assessment of disease estimates is hindered by problems in reporting of such studies. Despite a growth in published reports, existing guidelines relate to analytical rather than descriptive epidemiological studies. There are also no user-friendly tools (e.g., checklist) available for authors, editors and peer-reviewers to facilitate reporting of descriptive epidemiological studies for neurological disorders.

**Objective:** The Standards of Reporting of Neurological Disorders (STROND) is a guideline that consists of recommendations and a checklist to facilitate better reporting of published incidence and prevalence studies of neurological disorders.

**Methods:** A review of previously developed guidance was used to produce a list of items required for incidence and prevalence studies in neurology. A three-round Delphi technique was used to identify the ‘basic minimum items’ important for reporting, as well as some additional ‘ideal reporting items’. An e-consultation process was also used in order gauge opinion by external neuro-epidemiological experts on the appropriateness of the items included in the checklist.

**Findings:** Out of 38 candidate items, 15 items and accompanying recommendations were developed along with a user-friendly checklist.

**Conclusions:** We hope that the introduction and use of the STROND checklist will lead to more consistent, transparent and contextualised reporting of neuro-epidemiological studies and that these more applicable findings will lead ultimately to better healthcare decisions.
Session O4. Treatment/Management

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Long-Term Outcome of Vagus Nerve Stimulation in Children with Intractable Epilepsy
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Background: We evaluated the long-term outcome of children with intractable epilepsy treated by vagus nerve stimulation (VNS).

Methods: We analyzed 18 children (aged 4–18 years) with intractable epilepsy treated over a long period by VNS retrospectively. A vagus nerve device was implanted in the period of 2004–2011 and the children were evaluated at 1, 3 and 5 years after implantation. Seizure frequency was analyzed by clinical evaluation and interview. Efficacy was measured by the reduction in mean seizure frequency.

Results: The results showed that mean seizure reduction was 65% after 1 year, 69% at 3 years, and 71% at 5 years of age. One of 18 patients became seizure-free at 3 years of follow-up. No life-threatening adverse effects were seen.

Conclusions: In this study, long-term outcome of VNS treatment in children shows that VNS is an effective and safe treatment option in children with intractable epilepsy.

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Domestic Health Visiting: An Innovative Approach to Bridge Gaps in Epilepsy Care in Laos and Cambodia
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Objective: Epilepsy is a major neurological disorder and of particular relevance to Asia, as demonstrated recently (D Bhalla). The biggest challenge in epileptology lie in finding approach(s) that may effectively bridge the gaps in epilepsy care. Here, we present an innovative mechanism, named domestic health visiting (DHV), developed (D Bhalla) for increasing the access to care for those with epilepsy in two Asian countries-Laos and Cambodia.

Methods: This is a novel bi-centric interventional project being conducted in Laos and Cambodia. In each country, two sites (districts) are chosen, one being an interventional site (IS) and another being non-interventional site (NIS). In Laos the project locations are Pakgnum (IS) and Naxaythong and Sangthong (NIS). In Cambodia the project locations are Memot (IS) and O Reang Ov district (NIS). In IS, the intervention is DHV by domestic health visitors (DHv) through which population would be screened. Those screened would undergo diagnostic consultation at primary health centers (PHCs) by trained district hospital doctors. DHV would deliver treatment at-home at frequent intervals along with counseling and education of the patients. NIS would solely undergo mass-media through radio. In NIS, screening, diagnosis, treatment, and therapeutic follow-ups would be conducted upon an individual’s visit at PHCs & district hospitals which is the usual practice in these countries. At the end of 18-month follow up, various endpoints will be evaluated for possible changes between IS vs NIS and baseline vs final-line. The procedures that are being followed are given below.

Footnotes: DH: District Hospital; DD: District doctors; Dx: Diagnosis, HR: Human resources, KAP: Knowledge attitude practice, PHCs: Primary health centers.

Results: This is one of the very few examples where a public health program (with research aspects also) on epilepsy is being carried-out with Ministry of Health as one of the primary implementers. The benefits are aimed to go beyond people with epilepsy alone and touch upon service-providers (e.g. increased consultation) as well as health care system (e.g. trained staff and facilities). The precise variables that we are estimating a change are: Differences in the: – Total number of people that get screened (captured, identified) – Total number of people that get identified with epilepsy – Total number of contacts (+ contact hours) made between public and system – Total number of people that get treated during overall period – Total quantity of medicines used – Time to premature rupture of treatment – Treatment compliance – Premature mortality – Self-reported satisfaction with treatment – Difference in seizure frequency – Cost per-attendance Descriptive: – Number of epilepsy-compliant service facilities – Number of epilepsy trained human resource – Patient savings (in terms of negotiated price) – Increased political visibility – Availability of training material – Availability of public awareness materials – Number of people reached through mass-media.

Conclusion: The conclusion that we anticipate is that DHV becomes an effective and cost-conscious strategy to reduce diagnostic, treatment as well as the therapeutic follow-up gaps among people with epilepsy in Cambodia and Laos.

Session O5. Neurosurgery

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Outcome Following Craniotomy in Patients with Primary Intracranial Haemorrhage
Liew B.S.1, Azmin K.-R.2, Johar Siregan A.2
Department of Neurosurgery, 1Sungai Buloh, Malaysia; 2Jahor Bahu, Malaysia

Objectives: Primary intracranial hemorrhage or known as hypertensive intracerebral hemorrhage is one of the major health problems among productive workforce globally. It consists of 15 to 20 patients became seizure-free at 3 years of follow-up. No life-threatening adverse effects were seen.

Visitors (DHv) through which population would be screened. Those screened would undergo diagnostic consultation at primary health centers (PHCs) by trained district hospital doctors. DHV would deliver treatment at-home at frequent intervals along with counseling and education of the patients. NIS would solely undergo mass-media through radio. In NIS, screening, diagnosis, treatment, and therapeutic follow-ups would be conducted upon an individual’s visit at PHCs & district hospitals which is the usual practice in these countries. At the end of 18-month follow up, various endpoints will be evaluated for possible changes between IS vs NIS and baseline vs final-line. The procedures that are being followed are given below.

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Results: This is one of the very few examples where a public health program (with research aspects also) on epilepsy is being carried-out with Ministry of Health as one of the primary implementers. The benefits are aimed to go beyond people with epilepsy alone and touch upon service-providers (e.g. increased consultation) as well as health care system (e.g. trained staff and facilities). The precise variables that we are estimating a change are: Differences in the: – Total number of people that get screened (captured, identified) – Total number of people that get identified with epilepsy – Total number of contacts (+ contact hours) made between public and system – Total number of people that get treated during overall period – Total quantity of medicines used – Time to premature rupture of treatment – Treatment compliance – Premature mortality – Self-reported satisfaction with treatment – Difference in seizure frequency – Cost per-attendance Descriptive: – Number of epilepsy-compliant service facilities – Number of epilepsy trained human resource – Patient savings (in terms of negotiated price) – Increased political visibility – Availability of training material – Availability of public awareness materials – Number of people reached through mass-media.

Conclusion: The conclusion that we anticipate is that DHV becomes an effective and cost-conscious strategy to reduce diagnostic, treatment as well as the therapeutic follow-up gaps among people with epilepsy in Cambodia and Laos.

Session O5. Neurosurgery

683
Outcome Following Craniotomy in Patients with Primary Intracranial Haemorrhage
Liew B.S.1, Azmin K.-R.2, Johar Siregan A.2
Department of Neurosurgery, 1Sungai Buloh, Malaysia; 2Jahor Bahu, Malaysia

Objectives: Primary intracranial hemorrhage or known as hypertensive intracerebral hemorrhage is one of the major health problems among productive workforce globally. It consists of 15 to
20 percent of all hypertensive stroke. Patients suffered from hemorrhagic stroke tend to deteriorate faster than those with ischemic stroke. There is a very small window of time or golden hour for the initiation of acute medical and surgical managements in this group of patients to achieve better outcomes. Surgical treatments such as craniotomies and evacuation of blood clots are performed with very specific indications. Those patients with fast deteriorating conscious level, sizeable intracranial hematoma and fit to be subjected for a major cranial surgery under general anesthesia are usually candidates for such procedures, mainly for life-saving purposes. A very small group of patients undergo such procedures due to potential of reversal the motor deficits caused by the hematomas. This study is to determine the surgical outcomes of patients with spontaneous primary intracranial hemorrhage.

Methods: A retrospective study was conducted in a dedicated Neurosurgical Center at Hospital Sungai Buloh, Malaysia. The study was conducted for admission within a one year period (2013) with 6 months follow-up. A total of 35 patients who fulfilled the inclusion and exclusion criteria were studied. The significant value was set at p value less than 0.05. Odds ratio (OR) and 95% confidence intervals (CI) were calculated.

Results: The mean age was 52.8 years old (31–77 years old). A total of 29 patients (82.9 percent) were presented with putaminal hemorrhage, 4 with cerebral lobar hemorrhage (11.4 percent) and 2 with cerebellar hemorrhage (5.7 percent). The surgical mortality rate was 40 percent. At 6 months follow-up, 31.4 percent patients improved to Glasgow Outcome score (GOS) of 4, while 22.9 percent and 5.7 percent patients improved to only GOS of 3 and 2 respectively. There were several factors identified in the study to be important predictors of survival. There were statistically significant of higher mortality rate among patients with pre-operative Glasgow Coma Scale (GCS) of 5 and below (OR for death = 9.5; 95% CI 1.579 to 57.160; p = 0.015) and pre-operative CT scan brain showing acute hydrocephalus (OR for death = 4.267; 95% CI 0.992 to 58.335; p = 0.046). All patients with post-operative residual hematoma above 50 percent of pre-operative clots volume died (p = 0.006). Other factors such as age, size of pre-operative hematomas, intraventricular hemorrhage and underlying medical illness were not statistically significant in predicting the surgical outcome in those patients.

Conclusions: In this study, majority of patients who have undergone craniotomies were those with putaminal hemorrhage. Hence, we can conclude that surgical evacuation of hematomas in selected patients with putaminal hemorrhage may be beneficial. Pre-operative GCS and the presence of hydrocephalus in CT scan brain are important predictors which can be used by treating doctors to discuss with the patients’ family regarding their prognosis.

Objective: To study the carotid doppler findings in patients with anterior circulation ischemic stroke.

Methods: A retrospective analysis of carotid doppler findings in anterior circulation ischemic stroke patients admitted at Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow from June 2013 to July 2014 was performed. Electronic data and case record of all clinically and neuroimaging confirmed patients with ischemic stroke were analysed. The variables for analysis included demography, clinical features and risk factors. Patients with posterior circulation stroke and rheumatic heart disease were excluded. Stroke was classified using Oxfordshire community stroke project classification. The analysis of data was done to assess the risk factors and incidence of extracranial atherosclerosis in this subset of stroke patients. Extracranial atherosclerosis was assessed by carotid ultrasound and carotid intima media thickness (CIMT), plaque presence or absence and stenosis on ipsilateral as well as contralateral side to stroke were noted. The doppler findings were classified as normal CIMT, Increased CIMT with plaque and increased CIMT with stenosis of either common carotid artery (CCA) or internal carotid artery (ICA). A comparison of risk factors was also done between patients with or without narrowing of extracranial carotid arteries.

Results: The study included 55 patients [32 (58.2%) males, 23 (41.8%) females, mean age of 63.4 years]. Five (9.1%) patients had total anterior circulation infarction, 34 (61.8%) had partial anterior circulation infarction and 16 (29.15%) had lacunar infarction. Risk factor observed for atherosclerosis were hypertension in 39 (70.9%), diabetes mellitus in 18 (32.7%), dyslipidaemia in 40 (72.7%), smoking in 7 (12.7%), alcoholism in 5 (9.5%). Twelve patients (21.8%) had past history of stroke. Fifty (90.9%) patients showed abnormal doppler findings with increased CIMT in 41 (74.5%). Twenty five (43.6%) patients had increased CIMT with plaque (calcified or non-calcified) in Common Carotid Artery. Distal CCA or ICA narrowing was noted in 16/55 (29.09%) with severe narrowing >70% in 9 (16.4%) patients, while 12 (21.8%) had narrowing ipsilateral to stroke. Presence of diabetes mellitus was significantly associated with CCA or ICA narrowing (p = 0.03).

Conclusions: This study implies a high incidence of extracranial atherosclerosis in patients with anterior circulation ischemic stroke. The abnormalities were more marked in diabetics. The role of carotid doppler study as a non invasive tool in the identification of extracranial atherosclerosis is emphasized.
Objective: Vitamin B6 availability plays a critical role in both the innate and adaptive immune responses. A variety of disease conditions have repeatedly been found to be associated with low levels of vitamin B6. The aim of the study is to compare serum levels of tumor necrosis factor-alpha (TNF-α) and vitamin B6 among migraineurs when compared to healthy controls.

Methods: This hospital-based study was conducted in Hospital Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia, between January and December 2013. Migraine was diagnosed at the Neurology Clinic as per criteria of the International Headache Society. Inclusion criteria include: the patients between 15–60 years old and diagnosed with migraine for more than 1 year. Exclusion criteria include: pregnant women, migraine patients with any neurological, cardiovascular diseases and history of trauma. Serum was collected from a total of 129 female migraine cases and 129 non-migraine female volunteers. Vitamin B6 and TNF-α levels were measured using an enzyme-linked immunosorbent assay.

Results: Females with migraine had significantly lower vitamin B6 levels (10.9 vs 20.2 ng/ml, p < 0.001) but higher TNF-α levels (20.5 vs 3.9 pg/ml, p < 0.001) when compared with healthy controls. The significant Spearman’s correlation (0.42, p < 0.001) determined the moderate correlation between serum levels of vitamin B6 and TNF-α among migraine patients.

Conclusions: This study clearly indicates lower vitamin levels and higher TNF-α levels among migraineurs suggesting that inflammation may lead to lower levels of vitamin B6. Future studies should focus on intake of vitamin B6 and its effect on inflammation among migraine patients.
trode (parietal and temporal) locations. It shows that the task performance was good while listening to like-music (performing the task) when compared with hearing to dislike-music along task. In addition to that the percentage of error of commission for no go trials was less for like-music when compared to dislike-music. This clearly indicates the played dislike-music act as a distracter. Based on our findings, we conclude the subjects selective like-music can be used to improve the task performance.

Session O12. Basic and Translational Neuroscience

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Toll-Like Receptor 4 Deficiency Ameliorates Experimental Autoimmune Neuritis by Downregulating Classically Activated Macrophages (M1)
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Objectives: Toll-like receptors (TLRs) are a group of pattern recognition receptors sensing exogenous and endogenous deleterious signals. Activation of TLRs through the MyD88-dependent or MyD88-independent pathway triggers T helper (Th)1-oriented autoimmune responses by inducing production of IL-12 and tumor necrosis factor (TNF)-alpha. TLR4 is one of the most extensively studied members of the TLR family and has been associated with many autoimmune disorders.

Methods: Experimental autoimmune neuritis (EAN) was induced in TLR4 knockout (KO) mice and in C57BL/6 mice as wild type (WT) controls by immunization with P0 peptide 180–199 emulsified in Freund’s complete adjuvant. The effects of TLR4 deficiency on the clinical course of EAN and the functions of T cell and macrophages were studied.

Results: Toll-like receptor 4 deficiency remarkably ameliorated EAN. From day 15 post immunization, the clinical signs of TLR4 KO mice were significantly less severe than those of their WT counterparts. Upregulated expression of TLR4 was detected on the infiltrating cells in cauda equina of EAN WT mice and was correlated with the clinical scores. The proliferation of lymphocytes in response to either antigenic or mitogenic stimulation was attenuated in the KO mice. Nevertheless, TLR-4 deficiency downregulated the production of alternatively activated macrophage (M1), characterized by reduced production of interleukin (IL)-12 and nitric oxide (NO), and enhanced production of IL-10, both in vivo and in vitro.

Conclusion: Toll-like receptor 4 deficiency ameliorates EAN by downregulating classically activated macrophages (M1).

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Induced Alternatively Activated Macrophages (M2) Ameliorate Experimental Autoimmune Neuritis in Toll-Like Receptor 2 Deficient Mice
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Objectives: Toll-like receptors (TLRs) are a group of pattern recognition receptors sensing exogenous and endogenous detrimental signals. Activation of TLRs through the MyD88-dependent or MyD88-independent pathway triggers T helper 1 oriented autoimmune responses by inducing production of IL-12 and TNF-alpha. TLR2 is one of the most extensively studied members of the TLR family and has been associated with many autoimmune disorders.

Methods: Experimental autoimmune neuritis (EAN) was induced by immunization with P0 peptide 180–199 in TLR2 knockout (KO) mice and in C57BL/6 mice as wild type (WT) controls. The effects of TLR2 deficiency on the clinical course of EAN and the functions of T cell and macrophages were studied.

Results: Toll-like receptor 2 deficiency remarkably ameliorated EAN. From day 14 post immunization, the clinical signs of TLR2 KO mice with EAN were significantly milder than those of their WT counterparts. Upregulated expression of TLR2 was detected on the infiltrating macrophages in cauda equina of EAN WT mice and was correlated with the clinical scores. Although TLR2 deficiency did not alter the proliferation of lymphocytes in response to either antigenic or mitogenic stimulation, it induced an antiinflammatory phenotype of macrophages (alternatively activated macrophage, M2) characterized by reduced production of interleukin (IL)-12 and nitric oxide (NO), and enhanced production of IL-10.

Conclusion: Toll-like receptor 2 deficiency ameliorates EAN by inducing alternatively activated macrophages (M2).
Anti-CD73 Antibodies Are Sufficient to Prevent Rather Than Treat Experimental Autoimmune Neuritis

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Objectives: CD73 (ecto-5’-nucleotidase) is an ectoenzyme that produces adenosine. Since adenosine bears strong immunosuppressive and antiinflammatory properties, we hypothesized that anti-CD73 antibodies may aggravate experimental autoimmune neuritis (EAN), an animal model Guillain-Barré syndrome.

Methods: EAN was induced in C57BL/6 mice by immunization with P0 peptide 180–199 emulsified in Freund’s complete adjuvant together with pertussis toxin. Anti-CD73 monoclonal antibodies (2 g/kg body weight, once a day) were intraperitoneally administered either from the induction day of EAN (day 0 post immunization) as the prevention group, or from the onset of disease (day 8 post immunization) as the treatment group. Mice treated with PBS were used as controls.

Results: Anti-CD73 monoclonal antibodies were sufficient to prevent the onset of EAN. Mice in the prevention group did not develop EAN until day 50 post immunization. Correspondingly, sciatic nerve pathology (day 10, 30, 50, respectively) did not reveal evident inflammatory infiltration in the peripheral nerves, although the proportion of regulatory T cells (Tregs, CD4+CD25+FoxP3+ cells) in the spleen was reduced on day 28 post immunization (p < 0.01). However, the suppressive effects of anti-CD73 antibodies were not observed in the treatment group (p > 0.05).

Similar to the prevention group, Tregs in the spleen (CD4+CD25+FoxP3+) and in the peripheral nerves (FoxP3+) were reduced in the treatment group versus the control group, respectively at the peak of EAN (on day 28 p.i., p < 0.01 for both comparisons).

Conclusion: Anti-CD73 antibodies are sufficient to prevent rather than treat EAN.

Perception on the Utility of Screening Tools for Dementia in Malaysia

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Objectives: To determine the perception of three dementia screening tools in Malaysia among healthcare professionals and researchers.

Methods: A survey was conducted among health care professionals and researchers attending a workshop at the University of Malaya on the utility of the Identification and Intervention for people with Dementia in Africa (IDEA) Study Screening Instrument, Montreal Cognitive Assessment (MoCA) and the Picture-based memory impairment screen (PMIS) as memory screening tools for Malaysia. The survey respondents were asked to rate the three instruments after administering the questionnaires on each other. Each question was rated in a 4-point Likert scale.

Results: 32 participants (21 (61%) female), mean age±standard deviation = 31.50 ± 8.08, completed the survey. 28 (87.5%) were non-doctors, 17 (53.1%) worked in geriatric medicine and 15 (46.9%) had 5 or fewer than 5 years’ experience. Ninety-seven percent of respondents felt that the IDEA tool was a good or very good tool for dementia screening in Malaysia compared to 57% for MoCA and 78% for PMIS (p = 0.001). The proportion of respondents who selected good to very good for clarity of instructions and language were IDEA (97%, 100%), MoCA (75%, 81%) and PMIS (88%, 88%) respectively (p < 0.05). There was no significant difference in the proportion of respondents who selected good or very good for length of the three tools.

Conclusion: This was the first study which surveyed the perception of researchers and healthcare professionals on their opinion on screening tools used for dementia. The opinion of respondents in this pilot study suggested that researchers and healthcare professionals favoured the IDEA tool as a dementia screening tool in Malaysia, and for clarity of instructions and language.
Objectives: Migraine is one of the leading neurological disease and is a major public health issue. It is a great burden for the individual, the health care system and the society. Disability may be one of the main causes of burden contributing to poor quality of life (QOL) among migraine patients. Thus, this study was aimed to determine the primary factors associated with migraine disability among migraine sufferers.

Methods: This hospital-based study was conducted in the Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia between January and May 2013. Clinically diagnosed female migraine patients (n = 100) completed the Malay version of the World Health Organisation QOL Brief (WHOQOL-BREF) Questionnaire. The Malay version of the Migraine Disability Assessment (MIDAS) Questionnaire was only completed by migraine patients. Statistical analysis was performed using SPSS version 20.0.

Results: The migraine disability assessment score (OR = 1.92, CI = 1.36–2.73 p < 0.001), the total number of days with headache (OR = 1.51, CI = 1.24–1.83 p < 0.001) and pain score (OR = 1.37 CI = 1.06–1.76, p = 0.016) have significantly higher odds of causing more disability among migraine patients. The physical strength (OR = 0.84, CI = 0.73–0.96, p = 0.012) has significantly lower odds of migraine disability. The other individual domains such as social relationships, psychological and environmental conditions have lower odds of migraine disability even though these differences were statistically insignificant. Migraine patients with higher MIDAS score have 2.7 times higher odds of having disability (CI = 1.43–5.01, p = 0.002) when compared with patients with lower MIDAS score. At the same time, migraine patients with lower total QOL scores have 1.2 times higher odds of having disability (CI = 1.001–1.45, p = 0.049) when compared to patients with higher total QOL scores. Age has significantly lower odds while the duration of education has significantly higher odds of migraine disability among migraine patients.

Conclusions: This study clearly indicates that MIDAS score, lower total QOL and physical health score is significantly affect the disability among female migraineurs indicating that migraine pain may lead to severe disability. Therefore, measurement of QOL and MIDAS score may aid clinicians in assessing disability which can help in making appropriate prescribing choices for migraine pharmacotherapy.
Lifestyle Factors and Risk of Distal Myopathy: A Case-Control Study in Japan

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**Background:** Distal myopathy (DM) is progressive disorders characterized by weakness and atrophy of the voluntary distal muscles of the upper or lower limbs, and the involvement of gene variants is well established. However, the development of DM is thought to be also associated with environmental factors, not genetic factors alone. To the best of knowledge, few studies have reported the relationship between lifestyle factors and the risk of distal myopathy. We therefore analyzed the relationship between lifestyle factors and the risk of distal myopathy using a case-control study in Japan.

**Methods:** The study comprised 92 DM patients, and 393 gender- and age-matched controls (1:1–1:4) randomly selected from the general population. A structured self-administered questionnaire specifically designed for this case-control study was distributed and collected by mail in both patients and controls. We asked patients to recall their lifestyle within the 3 years before the onset of DM, and controls within the 3 years before the survey. The strength of association between DM and a potential risk factor was assessed by calculating odds ratios (ORs) and 95% confidence intervals (CIs).

**Results:** An increased risk of DM was significantly associated with type A behavior pattern, a less frequent intake of green vegetable, protein-rich foods such as egg, milk, meat and green tea. The greatest effect on risk for DM was posed by the combination of type A behavior pattern and less frequent intake of protein-rich foods.

**Discussion:** We found that the DM risk was significantly associated with type A behavior pattern as the excessive endogenous oxidative stress and a decrease in or lack of protection against muscle weakness and atrophy may affect the onset of DM.

**Conclusion:** The present study suggested that the manner and magnitude of the imbalance between an excessive production of oxidants and a decrease in or lack of protection against muscle weakness and atrophy may affect the onset of DM.
Increase of Cases with Narcolepsy After Pandemrix Vaccination in Östergötland County, Sweden

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Background: After the vaccination against swine flu with Pandemrix vaccine around 2009 it was demonstrated that the incidence of narcolepsy increased in several places in the western world, for example Finland, Sweden and Norway. In the county of Östergötland, like in some other counties in Sweden, the incidence of narcolepsy was calculated to investigate the magnitude of the increase.

Method: Patients with the diagnosis of narcolepsy were retrieved in the medical file system in all pediatric units in Östergötland (Norrköping, Linköping, Motala). Later the status of vaccination (performed in autumn 2009) was investigated. The cases were also entered in the Swedish National register of Narcolepsy, a quality register for monitoring the medical care.

Results: During 2000–2012 there were altogether 15 children that were diagnosed with narcolepsy. During the study period 2009–12 there were 14 diagnosed cases – one diagnosed case before vaccination and 13 afterwards. The incidence of narcolepsy in the period 2009–12 was 0.4/100,000 pre vaccination and 5.0/100,000 post vaccination. The percentage of new cases that were vaccinated was 93% (13/14). The age of onset was rather similar in the pre and post vaccination cases: 13 years of age pre vaccination and 12.4 post vaccination. The age distribution of cases in the post vaccination group was 4.4/100,000 in the age group 0–9 years, 10.3/100,000 in the age group 10–14 years and 5.8 in the age group 15–18 years. The gender ratio of all cases (14) were 7:7 (male/female) in all cases, 6:7 in the vaccinated cases.

Conclusion: The data from Östergötland add important information to the knowledge accumulated recently on the effect of Pandemrix on narcolepsy development.

Predictive Factors Associated with Severity of Carpal Tunnel Syndrome in Multiethnic Asian Patients

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Background: Carpal tunnel syndrome (CTS) is the commonest entrapment neuropathy referred for electro-diagnostic evaluation. Nerve conduction study (NCS) is useful to confirm the clinical diagnosis and to assess severity. However, the risk factors associated with development of severe CTS are still unknown.

Objective: To evaluate the risk factors associated with CTS and their relationship with the severity in nerve conduction abnormality.

Methods: A retrospective study of patients who were electrophysiologically diagnosed as CTS in Hospital Serdang, a tertiary medical centre in Malaysia during a 32-month period from October 2010 to May 2013. Patients were divided into 2 groups; non-severe and severe CTS. Factors, which include age, gender, ethnicity (Malays, Chinese and Indians), laterality of CTS, symptoms and diabetes mellitus were analyzed separately and compared with severity of CTS based on NCS.

Results: A total of 144 patients (102 females and 42 males) were recruited in this study; with age ranged from 18 to 76 years.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Non-Severe CTS N = 74 n (%)</th>
<th>Severe CTS N = 70 n (%)</th>
<th>Chi-Square</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Age &lt;60 Age &gt;60</td>
<td>60 (81.1) 14 (18.9)</td>
<td>55 (78.6) 15 (21.4)</td>
<td>0.023</td>
<td>0.879</td>
</tr>
<tr>
<td>Gender Male Female</td>
<td>22 (29.7) 52 (70.3)</td>
<td>20 (28.6) 50 (71.4)</td>
<td>0.023</td>
<td>0.879</td>
</tr>
<tr>
<td>Ethnicity Malay Chinese Indian</td>
<td>43 (58.1) 13 (17.6) 18 (24.3)</td>
<td>40 (57.1) 16 (22.9) 14 (20.0)</td>
<td>0.808</td>
<td>0.668</td>
</tr>
<tr>
<td>Symptomatic Symptomatic Non-Symptomatic</td>
<td>52 (70.3) 22 (29.7)</td>
<td>59 (84.3) 11 (15.7)</td>
<td>4.00</td>
<td>0.045*</td>
</tr>
<tr>
<td>Laterality Unilateral Bilateral</td>
<td>19 (25.7) 55 (74.3)</td>
<td>6 (8.6) 64 (91.4)</td>
<td>7.335</td>
<td>0.07</td>
</tr>
<tr>
<td>Diabetes Diabetic Non-Diabetic</td>
<td>13 (17.6) 61 (82.4)</td>
<td>25 (35.7) 45 (64.3)</td>
<td>6.098</td>
<td>0.014*</td>
</tr>
</tbody>
</table>

Data are reported as number of subjects with percent in parentheses.
Patients with diabetes mellitus were 2.5 times more likely at risk of severe CTS while the patients with bilateral CTS were 4 times more likely at risk to developed severe CTS. There was no significant association found between age, gender, ethnicity and symptomatic patients with the CTS severity.

Conclusion: Patients with diabetes mellitus and bilateral CTS are at risk in developing severe CTS. Severe CTS cases need to be treated urgently for better results. Thus we recommend that all the diabetic patients should be evaluated for CTS and early nerve conduction study is necessary to prevent delay in treatment and the associated disability.

Epidemiology Stroke Program in the Czech Republic – Is the National Registry of Hospitalized Patients Valid for Further Epidemiological Research?

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Objectives: Stroke is considered as a major cause of mortality and morbidity in East-Central Europe but valid epidemiological data are not available. As the first step to evaluate stroke epidemiology in the Czech Republic (CR) we validated the National Registry of Hospitalized Patients (NRHOSP).

Methods: NRHOSP is a nationwide registry, prospectively collecting information on each hospitalization in the CR since 1960. We randomly selected 10 hospitals and then 50 patients from each hospital admitted in 2011 stratified according to stroke diagnosis (ICD 10 codes I60, I61, I63, I64 and G45). Discharge summaries from hospitalization were reviewed by two independent reviewers and compared with NRHOSP for accuracy of discharge diagnosis. Any disagreements between reviewers and NRHOSP were adjudicated by a third independent reviewer.

Results: Of 500 requested discharge summaries, 484 were available for validation (response rate 97%). Stroke or TIA diagnosis (ICD code I6) recorded in NRHOSP was confirmed in 303 cases (62.6%, 95% CI: 59.6–65.7%). Of 385 cases coded in NRHOSP with stroke diagnosis only (I60, I61, I63 and I64) there were 326 cases (84.7%, 95% CI: 80.7–87.9%) confirmed with any of the stroke diagnoses (I60, I61, I63 and I64). Of these 326 cases, 255 (66.2%, 95% CI: 61.3–70.8%) were confirmed with the original stroke type diagnosis recorded in NRHOSP. With analysis by stroke type ischemic stroke I63 was confirmed in 80 of 98 cases (81.6%, 95% CI: 74.0–89.3%), subarachnoid hemorrhage I60 was confirmed in 88 of 97 cases (90.7%, 95% CI: 85.0–96.5%), and intracerebral hemorrhage I61 was confirmed in 86 of 95 cases (90.5%, 95% CI: 84.6–96.4%). TIA G45 was identified in 48 of 99 cases (48.5%, 95% CI: 38.6–58.3%). The single most important reason for disagreement between discharge summaries and NRHOSP was incorrect coding of unspecified stroke I64, which was reported to NRHOSP (in 95 cases) but in fact patients had specified stroke type (in 63 cases, 66.3%), TIA (in 10 cases, 10.5%) or another non-cerebrovascular diagnosis (in 21 cases, 22.1%).

Conclusions: The accuracy of coding of ischemic stroke I63, subarachnoid hemorrhage I60 and intracerebral hemorrhage I61 in NRHOSP were high. The data suggest that with appropriate consideration of stroke cases included in the unspecified stroke I64 and TIA G45 categories, the NRHOSP database can be utilized to provide high level epidemiological data regarding the occurrence of stroke in the Czech Republic. The data also suggest that the epidemiology of TIA (G45) in a population cannot be accurately assessed using data from an administrative database.

Establishment of Population Based Stroke Registry in Ludhiana City: Validation of the Methodology of Data Collection


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Objectives: We carried out a population based stroke registry using WHO STEPS methodology in the city of Ludhiana, India from August 2010 to March 2013. After the completion of the project we did a door-to-door survey to validate the methodology of data collected by WHO STEPS method. The objectives were (a) To compare the incidence of stroke between data obtained from population based stroke registry and by door to door survey method in Ludhiana city. (b) To validate the methodology of WHO STEPS approach by door to door method.

Methods: The door-to-door survey was conducted from August 2013 to October 2013. All stroke patients ≥18 years staying in the city for ≥6 months were included. According to 2011 census, the population of Ludhiana city ≥18 years of age is 10, 65, 127. The city is divided into 6 zones (Central, East, West, North, South and Atam Nagar) and there are 75 wards. Based on the 3rd year data obtained from the city (March 2012 to March 2013), we selected 3 areas using cluster sampling and the target population was 12,000. In the first step, we visited the houses of the stroke patients in all the 3 areas by taking the contact details from the stroke registry database. The demographic and stroke data was collected from the family members using the general family screening questionnaire. The screened positive patients were asked about the details of stroke including date of stroke, symptoms, risk factors and type of stroke (from investigations if available). Disability was documented using modified Rankin Scale (mRS) for the period 28 days after the stroke. A separate questionnaire was used to capture the stroke related mortality. The verbal autopsy questionnaire was used to screen stroke related deaths. Descriptive statistical measures were computed using SPSS version 21.0.
**Results:** A total of 6000 houses and 19051 subjects were covered from August 2013 to October 2013. The mean age of the population was 39 ± 15 years (range: 18–101 years) and 9820 (52%) were men. A total of 117 stroke cases were identified from the stroke registry database (March 2012 to March 2013). Out of 117 cases, we were able to contact 109 (93%) patients by door-to-door method and 8 (7%) subjects could not be contacted. Sensitivity and specificity of WHO STEPS approach method was 94.4% and 99.4% respectively. We missed 22 cases in the data collected by using WHO STEPS methodology (August 2010 to March 2013). The reasons of missing these cases were: patient went outside the city for treatment, visited general practitioners and indigenous system alternative medicine centres. The incidence rate in door-to-door survey is 142/100,000 as compared to the data collected by WHO STEPS methodology 140/100,000.

**Conclusion:** The sensitivity and specificity of WHO STEPS methodology was high. The incidence rate was similar in both the methodologies.

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**Poster Presentations**

**705**

**Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorders at a Single Tertiary Referral Center in Malaysia: A Hospital Based Study**

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**Objectives:** Epidemiological data about multiple sclerosis and related demyelinating disorders is lacking in Malaysia. The aim of this study was to look at the current demographics of this disorder in a multiracial country like Malaysia by looking at patients attending the Neurology Department at Kuala Lumpur Hospital which is the main tertiary referral center with Neurology services in the country.

**Methods:** This was a hospital based, retrospective study of consecutive patients attending the Neurology services at Kuala Lumpur Hospital. A registry method was used to collect data from consenting patients. Data was collected and analysed by a single neurologist. Patients were diagnosed with clinically definite multiple sclerosis (MS) or Mc Donald’s MS based on Mc Donald’s 20051 and 20102 criteria and neuromyelitis optica spectrum disorders (NMOSD) based on the Wingerchuk 2007 criteria.3 Patients with other idiopathic inflammatory demyelinating diseases (IIDDs) were excluded. The study period assessed retrospectively was from 2005 to 2014. Statistical analysis was done using SPSS version 16 software looking at descriptive data and medians.

**Results:** Out of 273 patients with IIDDs, 130 patients had clinically definite MS or Mc Donald’s MS and 93 patients had NMOSD. In the MS group, median age at onset was 31 years and there was a female preponderance ie, 81.4% females and 18.6% males with Female to male ratio of 4.4:1. In the NMO group, the median age at onset was 39 years with again female preponderance of 89.2% females and 10.8% males. Female to male ratio was 8.3 to 1. In the MS group, the racial groups affected in descending order were the Malays, 67 (51.5%), Indians 32 (24.6%), Chinese (25) 19.2%, followed by those of indigenous origin ie 1 Kadazan and 2 Ibans and 1 Bajau from East Malaysia and 2 of foreign descent. In the NMOSD group, the racial distribution was made up of Malays, 42 (45.2%), Chinese 42 (45.2%), Indians 7 (7.5%) and one each of Iban and Bajau descent.

**Conclusion:** The demographics of MS and NMOSD at our center mirrors the racial demographics in the country. More females were affected with both NMOSD and MS compared to males. MS and NMOSD were equally common in ratios of 1.4:1. More interestingly, we found NMOSD and MS to be equally common amongst the Malays but amongst the Chinese, NMOSD was more common with a ratio of 2 to 1. In the Indians, MS was commoner. For the first time, we see those of indigenous origin with MS and NMO. In summary, this study adds important demographic data for better understanding of these diseases in Malaysia.

**References**


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**711**

**The Association Between Estimated Glomerular Filtration Rate (eGFR) and Ischemic Stroke Subtypes:**

**Comparison Between Lacunar & Non-Lacunar Infarct**


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**Background:** Chronic kidney disease (CKD) is independently associated with an increased risk of developing lacunar infarct, an ischemic stroke subtype. The exact risk factors and mechanism of a lacunar infarct are not fully understood. The aim of this study was to determine if eGFR (calculated based on the Modification of Diet in Renal Disease Study formula) could be used to differentiate between lacunar and non-lacunar infarcts.

**Methods:** This was a comparative cross-sectional study based on analysis of secondary data derived from the stroke registry of UKMMC from October 2004 to December 2010. A total of 728 patients with acute ischemic stroke and known eGFR were included in the analysis.

**Results:** 277 patients with lacunar infarcts (38.0%) and 451 with non-lacunar infarcts (62.0%) were identified. Among the patients with lacunar infarct, 140 (50.5%) had diabetes mellitus, 224 (80.9%) had hypertension, 118 (42.6%) had dyslipidaemia and
63 (22.7%) were smokers. Conversely, among the patients with non-lacunar infarct, 219 (48.6%) had diabetes mellitus, 366 (81.7%) had hypertension, 188 (41.7%) had dyslipidaemia and 99 (22.0%) were smokers. There was no significant difference of these stroke risk factors between the two stroke subgroups. Univariate analysis also showed that there was no significant difference between the mean eGFR of lacunar and non-lacunar infarcts (54.3 ± 34.2 vs. 58.6 ± 62.5 mL/min/1.73 m², p = 0.29). Even when the eGFR was stratified according to the five CKD stages, this difference remained insignificant. Hierarchical multiple logistic regression based on the forced-entry method was used to test the possible effect of eGFR, once the other four stroke risk factors were controlled. Our analysis showed that eGFR was not a significant predictor (OR = 0.998; 95% CI = 0.994–1.002), even when the other factors were controlled. Although there was fulfillment of multivariate assumptions and goodness-of-fit, the model’s predictive value was poor and only explained 0.8% of the variance of the difference between the two groups.

**Conclusion:** eGFR was a poor predictor for differentiating between lacunar and non-lacunar infarcts in our population of stroke patients. This is probably due to the absence of unidentified confounding risk factors inside the model. A larger sample may also be required to ascertain a predictive role of eGFR.

### 722
**Comparison of Risk Factors Between Young Stroke and Older Age Group: Findings from a Hospital-Based Registry**


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**Background and Objectives:** Young stroke is defined as stroke occurring in those < 50 years of age and is commonly associated with conditions such as valvular heart disease, vasculitis or blood dyscrasias. The prevalence of conventional risk factors for atherosclerosis in young stroke is generally thought to be less compared to older stroke patients. Due to the high prevalence of hypertension, diabetes and dyslipidaemia in the Malaysian population generally we aimed to determine if our young and old stroke populations had similar risk factor profiles. We compared these two groups based on the stroke registry of UKMMC.

**Methods:** We analysed data of consecutive acute ischaemic stroke patients admitted between 2004 to 2010. Demographic data, risk factors and stroke subtypes were reviewed and analyzed. We compared the prevalence of risk factors between young stroke aged 18–49 year and older age group of >50 years.

**Results:** The proportion of young stroke in our registry was 9.9% (n = 82) from a total of 825 patients with ischaemic stroke consisting of 56 males and 26 females. Risk factors that were found to be significantly prevalent in the older age group include hypertension (83.2% vs 68.3%, p = 0.001), diabetes (57.2% vs 40.2%, p = 0.003) and dyslipidaemia (43.3% vs 30.5%, p = 0.025). Risk factors that were more prevalent in young stroke were smoking (34.1% vs 21.9%, p = 0.013) and a family history of stroke (15.9% vs 8.7%, p = 0.037). We also found a significantly higher proportion of males amongst the younger group (68.3% vs 51.1%, p = 0.002). Atrial fibrillation in our population was similarly represented in both young and old patients (13.0% vs 17.1%, p = 0.569). We also found that the prevalence of ischemic heart disease in both groups was similar. The commonest ischaemic stroke subtype in both age groups was lacunar strokes affecting 64.6% (n = 53) of young patients and 60.0% (n = 446) of older patients.

**Conclusions:** The proportion of hypertension, diabetes and dyslipidaemia is more significant in older patients based on our analysis. However, the high prevalence of these conditions in the younger age group suggests that our young strokes are at risk due to traditional vascular risk factors. Our data also suggests that the presence of these risk factors in the younger group is the result of lifestyle choices as more of them tend to be male and smokers. Campaigns focused on healthy living and lifestyle modifications may therefore assist in reducing the number of young stroke in our population. The effects of traditional vascular risk factors on the prevalence of young stroke in Malaysia warrants further study in a large population based assessment.

### 725
**An Analysis of the Clinical Risk Factors for Lacunar and Non-Lacunar Strokes in the Oldest Old Malaysians Population: Data from Hospital-Based Registry**


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**Background and objectives:** Ageing and lacunar stroke contribute to an increased risk of recurrent ischaemic stroke, white matter disease and cognitive impairment among the oldest old population (OOP) and ultimately lead to a significant caregiver burden. Determining and identifying which small deep infarcts are of lacunar and non-lacunar stroke aetiology and clinical risk factors are challenging, but important in order to deliver optimal stroke prevention therapy in the OOP. We sought to analyse the data from hospital-based registry the clinical risk factors after determining the lacunar and non-lacunar strokes in the oldest old Malaysians population.

**Methods:** A retrospective analysis was performed on the clinical risk factors for lacunar and non-lacunar strokes for patients of more than 80 years of age who were admitted between the year of 2004 and 2010.

**Results:** Out of 825 patients, 93 (11.3%) of them were >80 years old; 37 males, 56 females with mean ages of 84.1 and 84.5 years respectively. The most significant and prevalent of the OOP for ischaemic lacunar stroke was among male Chinese patients (51.5% vs 48.5%, p = 0.045, for male p = 0.007). The clinical risk factors identified to be prevalent but not significant in lacunar stroke...
among OOP were hypertension (57.1% vs 42.9%, p = 0.753), dyslipidaemia (63.6% vs 36.4%, p = 0.544), atrial fibrillation (54.5% vs 45.5%, p = 1.0), family history of stroke (80% vs 20%, p = 0.578), ischemic heart disease (57.1% vs 42.9%, p = 0.94) and recurrent stroke (68.2% vs 31.8%, p = 0.271). The clinical risk factors identified to be prevalent and significant in non-lacunar stroke among OOP was diabetes mellitus (55.0% vs 45.0%, p = 0.027). Smoking is otherwise, carries similar risk factor for both lacunar and non-lacunar strokes (50.0% vs 50.0%, p = 0.472).

Conclusions: Lacunar stroke is commoner than non-lacunar stroke among the oldest old Malaysians population notably among male Chinese patients. The most prevalent and significant clinical risk factor for non-lacunar stroke among OOP was the presence of diabetes mellitus. Earlier identification of these clinical risk factors might optimally deliver an optimal stroke prevention therapy which could lead to an improve quality of life and less caregiver burden and cost in this oldest old Malaysians population.

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Clinical Risk Factors for Lacunar Stroke in the Oldest Old Malaysian Population: Data from a Hospital-Based Registry

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Background and objectives: Lacunar stroke carries an independent risk of recurrent ischaemic stroke and cognitive impairment among the elderly. This leads to increased morbidity and significant caregiver burden. We sought to identify if differences exist in the risk factor profile of lacunar stroke in the oldest old patients (OOP) versus those below the age of 80. We analysed data from our hospital-based stroke registry to determine the prevalence of specific clinical risk factors and demonstrate difference of risk factor profiles in these two groups. This differentiation will allow delivery of optimal stroke prevention therapy in OOP with lacunar stroke, which will hopefully reduce the risk of recurrent stroke and cognitive impairment.

Methods: A retrospective analysis was performed on registry data of stroke patients who were admitted to our hospital between 2004 and 2010. Patients with lacunar stroke were identified and the group was dichotomized using 80 years of age as the discriminatory parameter. Those above 80 are classified as OOP.

Results: Out of 825 patients, 93 (11.3%) were >80 years old; 37 males, 56 females with mean ages of 84.1 and 84.5 years respectively. There were 54 lacunar strokes in this group compared to 445 in those 18–80 years (p = 0.612). Risk factors that were prevalent in OOP with lacunar stroke were hypertension (75%; p = 0.780), atrial fibrillation (11.8%; p ≥ 0.168), family history of stroke (5.4%; p = 0.154), ischemic heart disease (15.1%; p = 0.154) and recurrent stroke (23.7%; p = 0.556). However, the proportion of these risk factors in the OOP compared to those between 18–80 years of age was not statistically significant. In the younger group however, the prevalence of diabetes mellitus (57.0%, p = 0.019) and dyslipidaemia (44.1%, p < 0.001) were statistically significant compared to OOP. Smoking was equally prevalent in both age groups (p = 0.472).

Conclusions: Based on the analysis of our stroke registry, the majority of OOP were classified as having lacunar stroke. There were no risk factors that were found to be significantly prevalent in the older group, but we did find that diabetes and dyslipidemia were significantly prevalent in the 18–80 age group with lacunar stroke. Our findings suggest that in the OOP, prevalence of individual risk factors leading to increased risk of lacunar stroke is difficult to demonstrate. The increased risk of stroke is probably a composite/combination of these vascular markers and aging. However, this association would require investigation in a larger, community based sample before definite conclusions can be made.

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Demographics and Clinical Characteristics of Myasthenia Gravis in Multiethnic Population: A Malaysian Tertiary Centre Experience

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Background and Objectives: Myasthenia gravis (MG) is an immune mediated neuromuscular disease. A previous epidemiological study suggested that in the Malaysian population, demography and presentation of MG is influenced by ethnicity. Generally, there is limited data available on the epidemiology of MG in Malaysia. To date, no data has been published regarding thymic enlargement and its association with myasthenia gravis in terms of staging and treatment outcome. In this study, we investigated the clinical presentation of MG patients in UKMMC, looking at any ethnic variation in the age distribution compared to the bimodal pattern observed in the West. We also investigated the association between thymic enlargement in relation to MG staging, occurrence of myasthenic crisis and pharmacotherapy.

Methods: We conducted a retrospective analysis of secondary data derived from the the MG registry of patients admitted to UKMMC from 1980 to July 2014. A total of 122 patients were included. Diseases that mimic MG such as mitochondrial disease, congenital MG, Lambert-Eaton syndrome were excluded. The disease at onset was graded according to the Myasthenia Gravis Foundation of America (MGFA) Clinical Classification. Data on thymic enlargement on computed tomography (CT) thorax, frequency of myasthenic crises and use of immunosuppressants were obtained. The associations between stages of MG with thymic histology, myasthenic crisis and number of immunosuppressants were assessed and statistical analysis performed using SPSS version 20.

Results: A total of 122 MG patients' demographic and clinical characteristics were reviewed. Our group consisted 44.3% Malays, 51.6% Chinese, 1.6% Indian and 2.5% other ethnic groups. There

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was a female predominance (63.1%). In general, mean age of diagnosis for both genders was 47.95 years, showing a bimodal pattern of distribution—peaking at 30–35 years and at 60–65 years. The typical bimodal distribution of age was seen among female patients with mean ages of 30–35 years and 60–65 years old and presented at a younger age. Malay patients seem to follow the bimodal pattern seen in the West, with mean ages of 30–35 and 60–65 years at onset, which was not seen in Chinese patients. 51.4% patients had generalized MG and 48.6%, ocular MG. There were a significantly higher proportion of patients with thymic enlargement among those with generalized MG versus ocular presentation (35% vs 7%; p < 0.05). There was also significantly higher proportion of myasthenic crisis compared to those with ocular presentation (51% vs 8%; p < 0.01). The proportion of patients with generalized MG requiring immunosuppressant was significantly higher compared to ocular MG (p < 0.01).

**Conclusion:** In this hospital registry assessment, we found that the Malay and female population demonstrated the typical bimodal distribution as was reported in a previous study. Generalized MG was significantly associated with presence of thymic enlargement, occurrence of myasthenic crisis and the use of immunosuppressants. However, further analysis on histopathological finding will be useful to determine the correlation between thymic enlargements and disease outcome.

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### 741

**Evaluation of Modifiable Risk Factors for Stroke in Bangladesh: A Tertiary Level Hospital Experience**

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**Background:** There is limited study describing such stroke in tertiary level hospital experiences from developing countries like Bangladesh. Objectives: The aim study is to evaluate the modifiable risk factors stroke in both young and old age group.

**Methods:** A retrospective audit of medical records of all patients presenting between July 2011 to November 2012 with a stroke was conducted. Information about clinical presentation, modifiable risk factors laboratory and radiological investigations was collected. Data was entered and analyzed using SPSS14.0.

**Results:** Of total 183 cases 31 were young adults and 152 old patients between 18 to 100 years. Mean age young adult was 38.76 (± 6.379) and old age was 64.06 (± 11.238). 65.02% were male & 34.97% were female and the ratio was 1.9:1. Among patients majority had the Ischemic stroke in both age groups. In young age group 18 patients were diagnosed with ischemic stroke (58.06%) while 13 patients presented with hemorrhagic stroke (41.94%). In old age group 103 patients were diagnosed with ischemic stroke (67.76%) while 49 patients presented with hemorrhagic stroke (32.24%). Hypertension was the most common modifiable risk factor seen in both the young (54.8.0%) and in Old age group (55.9%), followed by previous history of transient ischemic attack (19.4%) and oral contraceptive pills (16.1%) in young age group and dyslipidaemia (23.7%), previous history of transient ischemic attack (20.4) and DM (19.7%) in old age group.

**Conclusion:** A high prevalence of modifiable risk factors such as hypertension in both groups in stroke patients was observed in the tertiary level hospital in Bangladesh.

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### Session P4. Treatment/Management

#### 712

**Determinants and Effects of Pre-Hospitalisation Delays in Stroke Patients in Universiti Kebangsaan Malaysia Medical Centre (UKMMC)**

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**Background and Purpose:** To determine the factors associated with pre-hospital delays in stroke patients and the prognosis of stroke in patients attending neurology clinic at UKMMC. We hypothesized that socio-demographic and economic factors were associated with pre-hospital delay and that longer pre-hospital delay was associated with poorer outcome.

**Methodology:** A cross-sectional study was conducted amongst stroke survivors attending the neurology out-patients clinic at UKMMC for the follow-up period of March to August 2014. We included patients who had been admitted to the UKMMC for an acute stroke from 3 months to 10 years prior. An administered questionnaire was used to determine if there was a delay in seeking medical attention and their contributing factors. The questions covered socio-demographics, socio-economics, medical conditions like hypertension, diabetes and previous history of Transient Ischemic Attack, what time of the day the stroke occurred and outcome measures.

**Results:** Among the 100 subjects who were enrolled in the study, 64% were male and 64% were aged >60 years. The median time from symptom onset to ED arrival was 2 (interquartile range 8.5) hours with 67% of the patients arriving before 4.5 hours. Delays in seeking treatment were more likely in patients with symptom-onset before midnight i.e. time between 7 pm to 12 am (P = 0.018, OR = 8.422, 95% CI 1.447–49.034) and in those with no previous history of transient ischemic attack (P = 0.044, OR = 0.17, 95% CI 0.021–0.978). Those who did not report a delay in seeking initial treatment accounted for 40.3% of the total. They were more likely to have a favorable outcome compared to those who were delayed (38.7%), but the difference was not found to be significant (OR = 0.936: 95% CI 0.391–2.238, P = 0.881). We also assessed if other factors such as age, gender, ethnicity, religion, level of education, household income, stroke severity, presence of an adult at the time of stroke mode of transport, referral from a clinic and seeking traditional/complementary treatment had an
Patients with tetrahydrobiopterin (BH4) deficiency develop not only hyperphenylalaninemia, but also neurological symptoms because of lack of catecholamine and serotonin. Since combination therapy with BH4 and neurotransmitter precursors (L-dopa and 5-hydroxytryptophan; 5HTP) was begun for BH4 deficiency in 1981 in Japan, 29 patients with BH4 deficiency have received BH4 and neurotransmitter precursors.

Objectives: We studied all patients with BH4 deficiency for 28 years and evaluated the efficacy and safety of BH4 and neurotransmitter precursors therapy from the newborn to the adulthood.

Patients: In all of 29 patients with BH4 deficiency, 26 were 6-pyruvoyl tetrahydropterin synthase (PTPS) deficiency and 3 were dihydopteridine reductase (DHPR) deficiency. Male were 15 and female were 14. As for the age category, under 3 years old were one, and between 3 and 15 years old were 7, and between 16 and 29 years old were 6. As for Biopten start age, under 1 year old were 14, and between 1 and 6 years old were 5, and between 7 and 15 years old were 2, and more than 16 years old were 8. As for the dosage for one day, less than 5 mg/kg were 17, and more than 5 mg/kg were 12. As for the combined medicine, L-dopa was 26 patients, and 5-HTP was 13 patients. It was one that used together the phenylalanine restricted diet.

Results: [Therapeutic efficacy] In all of 29 patients judgement of family doctor was ‘availability’ with the efficacy, and most cases maintained a normal range in serum phenylalanine (Phe) value. In PTPS deficiency serum phe levels were kept within control range (0.7–3.0 mg/dl) with the doses (1.5–13 mg/kg) of BH4 without diet therapy. In DHPR deficiency 2 patients showed serum phe levels of 2.4 and 4.6 mg/dl with the doses of BH4 of 3.8 and 2.2 mg/kg respectively, and one had slightly high serum phenylalanine levels (9.9–15.5 mg/dl) with the dose (16.9 mg/kg) of BH4, which was still remain control range.

Safety: There was only one event of adverse effect in one patient and the incident was 3.8%. It was a side effect of ‘the unfamiliarity’ without mention in precautions for use in one case of slight ‘both leg edemas’. However this patient (57 years old/a woman) had hypothyroidism and her leg edema was improved after supplementation of thyroid hormone. Therefore it was thought that safety did not have the new problem.

Conclusions: BH4 and neurotransmitter precursors therapy in BH4 deficiency was very effective to maintain serum phenylalanine levels within control range and a normal psychomotor development, and very safe from a baby to an adult for a long term. There were no serious adverse events that were thought to be related to not only Biopten but also L-dopa and 5HTP treatment at least for 17 years.
Dural Arteriovenous Fistula Presenting with Exophthalmos and Hemipaeresis with Seizures
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A concomitant focal seizure with left hemipaeresis and exophthalmos in the context of a malignant cavernous dural arteriovenous fistula (dAVF) is a variable neurological presentation. Here, we report a 73-years old female who presented with a 5-months history of progressive painless exophthalmos with conjunctival chemosis of right eye and now new onset of focal seizures with mild left hemipaeresis. Cerebral angiography demonstrated Cognard Type IIa right cavernous dAVF fed by branches from the right ascending pharyngeal artery and right middle meningeal artery, right accessory meningeal artery, bilateral arteries of foramen rotundum, dural branch of left vertebral artery with drainage to the right superior ophthalmic vein, right sphenoparietal sinus and right frontal cortical vein. Following transvenous embolization of the right cavernous via the right inferior petrosal sinus was done by using fibre coils and NBCA. Post-embolization Control angiogram showed complete obliteration of right cavernous dAVF feeding vessels, our patient had dramatic improvement of proptosis and chemosis along with cessation of clinical seizures and neurological improvement.

Neuroresuscitation Simulation Training Courses in Japan
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Background and Aims: In neurological emergencies, the appropriate general management of unconscious patients should be performed to minimize second brain damage and maximize patient recovery. These skills of general management in neurological emergencies were defined as 'neuroresuscitation' in Japan and published as a guideline in 2010. Furthermore several simulation training courses have been developed in Japan to learn the skills of neuroresuscitation. We reported one of these simulation courses, Primary Neurosurgical Life Support (PNLS) course, developed in 2009. Both courses are designed for a half-day course because all-day course is too long for most doctors and nurses concerned in neurological emergencies. They consist of 4 modules, Module A, evaluation of consciousness levels; Module B, evaluation of neurological conditions; Module C, management of cerebral herniation using simulated patients; and Module D, group work study of neuroresuscitation using clinical maps, developed as a tool for case simulation at a desk. ISLS is focused on stroke and PNLS is focused on neurosurgical emergency. 600 ISLS courses and 20 PNLS courses have been conducted so far.

Conclusions: Neuroresuscitation simulation training courses are very useful tool for medical staffs in neurological emergencies. We are planning a new simulation training course for acute neurological dysfunction.

Session P6. Neuro-Rehabilitation

Brain Computer Interface for Gaming Applications
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Background: Brain computer interface can be defined as contact pathway between a person and their external surroundings with the support of EEG signals. BCI basically uses brain activity during the process of imagination and they find wide applications in neuro rehabilitation, and in various gaming application for training subjects. Motor imagery is associated with power changes in the acquired EEG signals due to event related De synchronization in the motor cortex areas. In the present BCI system decisions were made based on very short segments of recorded EEG data.

Methods: The electrical activity of the brain was acquired by means of electrodes placed on the scalp at sensory motor cortex during imagination. The key feature analyzed was the Mu wave suppression and is observed in the EEG signal band (8–14 Hz) during motor action and intended movements. The EEG signals were acquired for six subjects and correlation was established between the EEG signals acquired during actual and imaginary hand movements by extracting the suppression of Mu wave during actual and intended hand movement. The extracted was used as a control signal to navigate in the game environment.
Results: A Spearman’s Rank Order correlation was used to determine the relationship between imaginary and actual left hand movement. There was a positive correlation between imaginary and actual left hand movement (rs(6) = 0.786). The non-parametric Wilcoxon Signed rank test was used for comparing the Mu power suppression observed during actual and real time hand movement. The Event Related De synchronization during task and rest showed a statistically significant change during actual left hand movement (p = 0.028).

Conclusion: Throughout imaginary right and left hand movements the suppression of Mu rhythm occurs similar to actual hand movement. In additional to that the contra lateral activity (suppression of Mu power in opposite electrodes – i.e C3-CZ for right hand movement and C4-CZ for left hand movement) was established. By means of all these data the control signals were extracted for the gaming application using simple seeker destination pathway simulated using Java. It will serve as a creative tool that can be used in future for rehabilitation purposes.

Conclusions: To date, acute myocardial infarction is noted to be one of the complications of AD however, it could be the precipitating cause of AD and the myocardium pain may exaggerate the spinal stretch reflex activity subconsciously and leading to myoclonic jerky movement. Thus, acute MI should be considered as a precipitating cause of AD to reduce morbidity and mortality.

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To Study the Correlation between Clinical Spasticity and Urine Hydroxyproline/Muscle Hydroxyproline among Children with Cerebral Palsy – A Future Clinical Implication

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Background: Hydroxyproline is a major component of the protein collagen and muscle hydroxyproline (MH) level correlates with severity of the spasticity. Urine hydroxyproline (UH) excretion is a fairly sensitive indicator of collagen breakdown and can be used at the clinical level to predict collagen changes.

Aim: To compare the MH, UH level in spastic CP children with normal control group and determine the correlation between clinical spasticity with that of UH.

Method: This was a cross sectional comparative study, conducted in tertiary centre. Children with spastic CP (6 to 18 years) who were scheduled for muscle/tendon lengthening as part of the ongoing management for contracture and CP children with pure spasticity were included in this study. Muscle biopsy and urine samples were collected for HYP analysis.

Results: Total of 52 children (Normal children: n = 20, CP children with contracture: n = 16, CP children with pure spasticity: n = 16) were included in this study. The reducing trend in UH level was noted in contracture group in comparison to normal group. Mann-Whitney U test was used for data analysis. Mean hydroxyproline levels in random urine samples was 13.612 mg/ml while the mean muscle hydroxyproline levels from the same patients was significantly higher at 183 mg/ml (p = 0.000). There was a significant correlation between Modified Ashworth Scale (clinical spasticity) and random UH among 2 groups (contracture and pure spasticity) (p = 0.001).

Conclusion: UH can be considered as a tool to correlate with severity of the spasticity. Collagen accumulation outweighed the collagen breakdown and it could be the reason for reduced UH in CP children with contracture. A larger sample analysis is required to determine the significant association between contracture/pure spasticity and UH level. Expansion of the study on enzymes responsible for collagen breakdown such as matrix metalloprotease (MMP) will give more precise explanation and may help with future management plans.

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**Poster Presentations**

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Unusual Presentation of Autonomic Dysreflexia in Patient with Cervical Spinal Cord Compression – Is Myocardial Infarction a Cause or an Effect?

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Background: Autonomic Dysreflexia (AD) is not an uncommon clinical condition and it is usually detected in patient with complete spinal cord injury at or above thoracic 6th (T6) vertebrae with an incidence of 48–60%. This is a case report of a patient with cervical spinal cord injury (CSCI) with unusual presentation of autonomic dysreflexia (AD) associated with acute myocardial infarction (AMI) and myoclonic jerk.

Aim: To further describe the unusual presentation of AD and highlights the possibility of cardiac event as a cause or an effect especially in mentally challenged patient with cervical spinal cord injury.

Methods: This case was reported in Tertiary hospital, Kuala Lumpur, Malaysia. A 52-year-old mentally challenged male patient presented with all 4 limbs weakness especially on the right side after he fell down from the stairs in sitting position. MRI showed cervical OPLL (Ossified Posterior Longitudinal Ligament), worst at C3/C4 level, causing significant spinal cord compression and edema. He underwent anterior cervical corpectomy and fusion with removal of OPLL.

Results: On post-operation day 9, patient developed sudden onset of myoclonic jerks in both upper limbs and lower limbs associated with profuse sweating at face, neck and shoulder. His blood pressure was 172/104 mm Hg and pulse rate was 88 min. He was noted to have a distended bladder with over 1 L of urine. CT brain was normal. Mild hyponatremia (129 mmol/l) was noted. ECG showed inferior myocardial infarction.

Conclusion: To date, acute myocardial infarction is noted to be one of the complications of AD however, it could be the precipitating cause of AD and the myocardium pain may exaggerate the spinal stretch reflex activity subconsciously and leading to myoclonic jerk movement. Thus, acute MI should be considered as a precipitating cause of AD to reduce morbidity and mortality.
Application of Aremo Device in Treatment of Dysgraphia and Other Developmental Dysability
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After experienced stroke, traumatic brain injury, or other neurological or muscular damages, large numbers of patients still do not have neuromuscular control in hemiparetic extremity. Because of the weakness of muscles and inability to conquer with gravity, usage of arm is disabled. Armeo neutralizes weight of arm, enable usage of remaining control in both arms and hands by following exercises which represent real life situations in 3D simulations. Software accepts trajectory of patient's arm and wrist movement and with that enables therapists to evaluate patient’s pattern of coordination and improvement during treatment. Device is easily adaptable to patient's needs and it is possible to be used also without help of therapist. Armeo speeds up re(habilitation) by combining adaptable support for arm with grabber which is very sensitive and stimulates everyday activities. Data's for every patient can be electronically archived, which enables evaluation and follow up of improvements in treatment. Application of Aremo in situations with head injuries described till now can be widen, for the first time by our opinion, on application of Armeo in habilitation and early stimulant treatment in children with graphomotor dysgraphia, dyspraxia, cerebral paralysis (CP), autism and intellectual dysability, with respect to hypotonic muscular hand and inadequate coordination. By seasonable application of this device in treatment of these children, their hand and arm motoric can be improved, which would definitely affect quality of their everyday activities and ability to learn and carry out school tasks.

Session P9. Neuropharmacology

Evaluation of Pharmacotherapy for Developmental Disorder
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Purpose: Children with developmental disorder often suffer from epilepsy and paroxysmal EEG abnormality. In pharmacotherapy for developmental disorder, not only anti-psychotic drugs, a combination of anti-epileptic drugs have an effective for behavioral and psychiatric symptoms in many cases. Evidence of pharmacotherapy for developmental disorder associated with abnormal EEG has not been established. Purpose of this study is to evaluate the usefulness of anti-epileptic drugs in developmental disorder, which showed EEG abnormalities with or without clinical epileptic seizures.

Method: A total of 143 patients of developmental disorder (autism spectrum disorders: ASD, attention deficit hyperactivity disorder: ADHD, intellectual disability: ID), who have been treated and followed-up at our outpatient hospital (from 3 to 28 years, mean age 12.8 years) were included in this study. Each participant’s EEG had been recorded approximately every 6 months under sleep conditions. We examined for the therapeutic effect including of behavioral and psychiatric improvement to anti-epileptic drugs.

Results: EEG abnormalities were present in 76.0%, epilepsy was complicated in 55.0% of ASD. EEG abnormalities were complicated in 75.0%, epilepsy was complicated in 25.0% of ADHD. All patients showed EEG abnormalities on frontal areas. Although, there is no statistically significant difference in the effectiveness of anti-psychotic drugs or anti-epileptic drugs, all patients in the both combined patients were more improved. VPA and CBZ is widely used as a mood stabilizer in children with developmental disorder, particularly among those with seizure disorders and abnormalities in the EEG. In ADHD, EEG improvement with anti-epileptic drug treatment showed a high correlation with behavioral improvements as shown by ADHD-RS and GAF scores. In ADHD, EEG improvement with anti-epileptic drug treatment showed a high correlation with behavioral improvements and EEG findings.

Conclusion: EEG abnormalities were present in 76.0%, epilepsy was complicated in 55.0% of ASD. EEG abnormalities were complicated in 75.0%, epilepsy was complicated in 25.0% of ADHD. All patients showed EEG abnormalities on frontal areas. Anti-epileptic drug is effective in developmental disorder who had EEG abnormalities even though without clinical epileptic seizures. In the cases of poor effect of anti-psychotic drugs associated with EEG abnormalities, anti-epileptic drugs may be an alternative treatment in developmental disorder. It is necessary to review by the quantitative behavioral and EEG assessment after treatment of anti-epileptic drugs as an issue in the future by prospective intervention.

The Role of Interaction Between Cannabinoid and Vanilloid Systems on Hippocampal Synaptic Plasticity in Rats
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Long-term potentiation (LTP) has been most thoroughly studied in the hippocampus, which has a key role in learning and memory. Endocannabinoids are one of the endogenous systems that modulate this kind of synaptic plasticity. It has been reported that delta-9-tetrahydrocannabinol (Δ-9-THC), the major pharmacologically active molecule found in the plant Cannabis sativa, bind two types of G-protein-linked cannabinoid receptors (CB1 and CB2) that have been identified using molecular and...
pharmacological approaches. Cannabinoids are produced throughout the brain and CB1 receptors are particularly well represented in the cortex (entorhinal and cingulate), hippocampus, lateral septum, nucleus accumbens, amygdala, and periaqueductal gray area. The activation of the vanilloid system has also been shown to mediate synaptic plasticity in the hippocampus. In addition, immunohistochemical studies have shown that CB1 receptor and vanilloid receptor 1 (TRPV1) are closely located in the hippocampus. In this study, we examined the hippocampal effects of co-administering WIN55-212-2 and capsaicin, which are CB1 and TRPV1 agonists, respectively, on the induction of LTP in the dentate gyrus (DG) of rats. Rats were anesthetized intraperitoneally with urethane (1.5 g/kg with supplemental injections as required) and fixated in a stereotaxic apparatus for surgery. A heating pad was used to maintain the animals’ body temperature. After incision of the skin and obtaining the position of the DG according to the Paxinos and Watson atlas for the rat brain, small burr holes were drilled in the skull. Recording and stimulating electrodes were positioned in DG [AP: −3.8 mm from bregma; ML: 2.3 mm from midline; DV: 2.7–3.2 mm from the skull surface] and perforant pathway (PP) [AP: −8.1 mm from bregma; ML: 4.3 mm from midline; DV: 3.2 mm from the skull surface] respectively. The electrodes were lowered very slowly (0.2 mm/min) from cortex to hippocampus, in order to minimize trauma to the brain tissue and field potential recording were obtain in the granular cells of the DG following stimulation of the PP. Electrode positions were optimized to record maximal population spike (PS). LTP in the hippocampal area was induced by high-frequency stimulation (HFS). Data were statistically analyzed by repeated measures ANOVA tests followed by Tukey’s test. Values of p < 0.05 were considered to be significant. Our results indicated that the cannabinoid agonist reduced both field excitatory post-synaptic potential (fEPSP) slope and population spike (PS) amplitude after HFS with respect to the control group, whereas the vanilloid agonist increased these parameters along with the increased induction of LTP as compared to the control group. We also showed that the co-administration of cannabinoid and vanilloid agonists had different effects on fEPSP slope and PS amplitude. It seems that agonists of the vanilloid system modulate cannabinoid outputs that cause an increase in synaptic plasticity, while in contemporary consumption of two agonist, TRPV1 agonist can change production of endocannabinoid, which in turn result to enhancement of LTP induction. These findings suggest that the two systems may interact or share certain common signaling pathways in the hippocampus.

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**Session P10. Neuropsychology**

**733 The Frequency of Atypical Articulation in Preschool Children**

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**Objectives:** Research of typical and atypical articulation of sounds and articulation disorders represent actual problem, since this provides insight into the movements of articulation votes in younger school age children, as well as the ability to produce speech in children of this age, which can lead to early identification, diagnosis and treatment these disorders. Typical pronunciation implies that the child, when pronunciation sounds in speech segments, reaches for the sounds typical pronunciation what they have grown in their environment. However, this does not mean that the pronunciation of a completely automated. If the realization of phonemes, in any dimension, goes beyond the standard set boundaries, it is the unusual articulation, whereby the deviation may be apparent to one or a set of articulation and/or acoustic characteristics. The main goal of frequency for disorders of articulation is the development and formation of skills and habits of correct pronunciation of the sound.

**Methods:** Sample consisted of 316 children, aged five years. The subjects were tested with the Global articulation test, to assess the status of articulation. After that, all children with atypical articulation (101 children) were tested with the Test of oral praxis and language tests (Test of verbal memory, Test of nouns of the first level of abstraction, Test of nouns of the second level of abstraction, Test of prepositions and adverbs).

**Results:** In our study, children aged five years, atypical articulation was observed in 31.96% of the children, and in relation to sex, is more prevalent in girls. The most common atypical-articulated sounds are: laterals (l, lj), fricatives (t, s, z, š, ž), affricates (ć, č, đ, ď) and plosive (t and d).

**Conclusion:** The most common type of atypical articulation is lambdacism and follow rhotacism, expanding sigmatism, sigmatism and least represented are thetacism and deltaxism. In most cases the distortions are present, representing a milder form of atypical articulation. With the number of groups of atypical articulated sounds, there is an increasing the length of speech therapy.
The Frequency of Dysgraphia in Slovakian – Serbian Bilingualism

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Objectives: Slovakian-Serbian bilingualism represents special segment of language situation of Slovakian community. Slovakian language community in Vojvodina (Serbia) has geographical character of not so compact ethnic enclave which has been developing for 200 years as special, geographically separated part of Slovakian community. It represents about 3% of total number of inhabitants in Vojvodina, whose main characteristic is active Slovakian-Serbian bilingualism. The goal of this research was to determine frequency of dysgraphia in children of Slovakian nationality.

Methods: The sample of this research consists of 170 children of both genders. Examined are bilingual children of Slovakian nationality, of second, third and fourth grade. For assessment of dysgraphia of handwriting in this research it is used Test for the assessment of dysgraphia in handwriting (Cordic and Bojanin, 1992). Test was adjusted to the bilingual children of Slovakian nationality, and embraces writing by the dictation with script written on Slovakian language, free essay with subject ‘One experience of mine’ (Slovakian ‘Jeden môj zážitok’), transcription of text, and drawing of human figure. Text for the dictation which is adjusted for bilingual children is translated to Slovakian language, and consists of all letters of Slovakian language.

Results: Obtained results show that frequency of dysgraphia is 13.5% of children in Slovakian-Serbian bilingualism. Results show that frequency of appearance of dysgraphia in examined boys of Slovakian nationality is significantly higher than in girls. The most of children with dysgraphia is in third grade, 19.1%. In second grade is smaller percentage of children, 16.9%, while the lowest percent is identified in fourth grade, 7.2%. Also, in this children is more frequent dysgraphic-dyslexic dysgraphia (Golubovic S. 2000, 2011, 2012), in 65.20%, while graphomotor dysgraphia is less expressed, i.e. in 34.80% of cases.

Articulation Disorders in Children of Preschool Age with Hyperbilirubinemia on Birth

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Objectives: The goal of this research was to examine possible influence of risk factors on occurrence of articulation disorders in children of preschool age. Also, it was examined if there was difference between articulation of sounds in boys and girls regarding the level of bilirubin and Apgar score.

Methods: Sample for this research consisted of 100 children, of both genders, who had systematic control in Health center Arandjelovac, age of 6 and 7 years, 48 girls and 52 boys. Half of sample consists of children of preschool age who had bilirubinemia on birth. Research was done during March, April and May of 2013. For determining Apgar score and level of bilirubin in prenatal period there were used data’s from health cartons of children, and data’s obtained from parents. For determining the articulation status it is used Global Articulation Test (Kostic D), Vladisavljevic S, 1983).

Results: Obtained results show that large number of sounds in Serbian language in preschool children was distorted, while all children correctly pronounced sounds from group of vowels, nasals, plosives, as also half-vocal ʃ. The biggest deviation in articulation of sounds are in fricatives (38.97%), affricates (36.76%), laterals (17.64%), and vibrant r (6.61%), while lateral lj was in utmost percent distorted. Articulation disorders are more frequent in boys (36%) than in girls (24%), and larger number of boys with articulation disorder (38%) had high bilirubin on birth, while 33% of girls with hyperbilirubinemia on birth had articulation disorder. Utmost percent of articulation disorders is in children whose level of bilirubin on birth was between 150 and 200 mol/l. In these children with high level of bilirubin on birth more frequent is disorder of pronunciation of sounds V, G, Z, K, Lj, H, F. Articulation of sounds: Đ, Ž, Ľ, Lj, R, S, Ć, Š, Č, Dž, C is the most frequently disordered in children whose Apgar score was 9, while articulation of sounds: H, G, Đ, K, Ć, F, V is the most frequently disordered in children whose Apgar score was 7.

Neuroprotection of Rapamycin Against Parkinson’s Disease Neurotoxin Rotenone in Primary Mesencephalic Cell Culture

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Background: Parkinson’s disease (PD) is the most common movement disorder characterized by progressive and extensive loss of dopaminergic neurons in substantia nigra pars compacta (SNpc) and their terminals in the striatum (Park and Lee, 2006). So far, only symptomatic treatment using levodopa is available and no cure or disease modifying drugs exist (Boll et al., 2011).

Objectives: The present study was designed to investigate neuroprotective potential of rapamycin, a specific autophagy inducer, on dopaminergic neurons against rotenone-induced cell death in primary mesencephalic cell culture relevant to PD.
Fig. 1. For Abstract No. 584.

Fig. 2. For Abstract No. 584.
Methods: Primary mesencephalic cell cultures were prepared from OF1/SPF embryos at gestation day 14 according to Radad et al. (2010). On the 10th day in vitro (DIV), three different sets of cultures were kept untreated, treated with 20 nM of rotenone for 48 h, and co-treated with rapamycin (1, 10, 100, 1000 nM) and rotenone for 48 h, respectively. On the 12th DIV, cultures were subjected for immunohistochemistry against tyrosine hydroxylase, and fluorescence staining using Lysotracker Deep Red, JC-1 and DAPI stains.

Results: Treatment of cultures with 20 nM of rotenone on the 10th DIV for 48 h decreased the number of dopaminergic neurons by about 41% (Fig. 1, 2A) and increased the release of lactate dehydrogenase (LDH) by 178% compared to untreated controls. Against rotenone, rapamycin (100 nM on the 10th DIV for 48 h) increased the number of dopaminergic neurons by 17.42% (Fig. 1, 2A) and decreased the release of LDH by 64.20% compared to rotenone-treated cultures. Using Lysotracker Deep Red fluorescent dye showed that rapamycin increased lysosomal activity and formation of autophagosomes in the cultured cells as indicated by the higher red fluorescence (Fig. 2B). Rapamycin as well significantly increased mitochondrial membrane potential (∆ψm) as it increased red:green fluorescent ratio of JC-1 (Fig. 2C). Moreover, rapamycin decreased rotenone-induced apoptotic cell death in primary mesencephalic cell cultures as shown by the blue-fluorescent DAPI nucleic acid stain (Fig. 2D).

Conclusion: Taken all together, our study indicated for the first time that rapamycin protected dopaminergic neurons against rotenone-induced cell death in primary mesencephalic cell culture.

References

Ageing is a continuous progress throughout the individual’s life. Unlike pathological conditions, the ageing process affects all individuals. It is a process that is genetically programmed but modified by environmental influences, so the rate of ageing can vary widely among people. The physical condition of the individual can radically affect the measurements of cardiovascular function in the elderly and physical activity profoundly affects cardiovascular functions. Physiologic aging is characterized by gradual loss in function in many organ systems. Photoplethysmography (PPG) is a simple and low-cost optical technique that can be used to detect blood volume changes in the micro-vascular bed of tissue. Analysis of finger PPG has been widely used in clinical physiological measurements, including clinical physiological monitoring, vascular assessment and autonomic function.

Objective: Establishing a noninvasive, low cost vascular risk screening tool for cardiovascular event monitoring.

Method: A total of 332 subjects participated in data acquisition activity in the duration of the research. Twenty of these subjects underwent repeatability recording for between two to six different

Fig. 1. For Abstract No. 731.
sessions. The quantification of the vascular risk will provide a clear measure of vascular performance. Empirical Data Modeling was initiated by similarity-studies between the PPG waveform components and characteristic in classifying the following factors, ageing and cardiovascular risk. These analyses have been the basis for the single pulse selection representing the health index of a subject, which was used as benchmark to establish the vascular risk prediction index through exponential and logistic regression model. A repeatability and variability study was conducted on ten randomly selected subjects in further establishing the single pulse usage that produces repeatability coefficient, $CR = 93.22 \pm 1.18$ and variability coefficient, $CV = 6.18 \pm 1.51$.

**Result:** The proposed vascular risk prediction model has produced the following results: i. The sensitivity/specificity in classifying risk is 100.0%/100% for ages from 20 to 44 years and 85.7%/95.2% for ages from 45 to 66 years old, respectively. ii. The $r$-square value is 0.8226 for age (20–44) and 0.9205 for age (45–66) years old.

**Conclusion:** Such an estimation of a vascular health index may help in early detection of cardiovascular related diseases by exposing risk very early via non-invasive and low-cost device.

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**Session P17. Public Health**

**766 Development Process of Neuroresuscitation Guidelines in Japan**

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**Objectives:** Japan Resuscitation Council (JRC) developed the first and original resuscitation guideline on acute care of neurological diseases with epidemiological approach, as neuroresuscitation (NR) in 2010. Process of development of NR is presented.

**Methods:** For development of NR, JRC organized NR special interest committee in 2008. The committee is consisting emergency physician, neurologist, neurosurgeon, anesthesiologist, epidemiologist. The committee developed contents and guidelines of NR. Contents of NR is appeared on JRC Web Site: http://jrc.umin.ac.jp/pdf/20121022_NR_E.pdf English translation of NR is in process.

**Contents:** I Overview. II Neurological manifestations at around resuscitation (adults). 1) Acute consciousness disturbance 2) Status epilepticus. 2-1) Generalized convulsive status epilepticus. 2-2) Nonconvulsive status epilepticus. 3) Raised intracranial pressure and Brain edema III Diseases and conditions which needs neuroresuscitation (adults). 1) Cerebrovascular diseases. 1-1) Prehospital care. 1-2) Initial management before final diagnosis. 1-3) Cerebral infarction. 1-4) Intracerebral hemorrhage. 1-5) Subarachnoid hemorrhage. 1-6) Other cerebrovascular diseases. 1-6-1) Cerebral arterial dissection. 1-6-2) Stroke with aortic dissection. 1-6-3) Cerebral venous/sinus occlusion. 4) Acute encephalopathy. 2-1) Diabetes-related encephalopathy. 2-2) Hepatic encephalopathy. 2-3) Uremic encephalopathy. 2-4) Pulmonary encephalopathy. 2-5) Septic encephalopathy and Sepsis-associated encephalopathy. 2-6) Pancreatic encephalopathy. 2-7) Wernicke encephalopathy. 2-8) Encephalopathy related to hypotension. 2-9) Central and extra-pontine myelinolysis. 2-10) Paraneoplastic syndrome. 2-11) Drug-relatedencephalopathy. 2-12) Reversible posterior leukoencephalopathy syndrome. 2-13) Postcardiac operation encephalopathy. 3) Infection of the central nervous system. 3-1) Herpes simplex virus encephalitis. 3-2) Bacterial meningitis. 3-3) Tuberculous meningitis. 3-4) Anti-NMDA (N-Methyl-D-Aspartate) receptor encephalopathy. 4) Acute neuromuscular diseases. 4-1) Guillain-Barré syndrome. 4-2) Myasthenia gravis. 5) Neuroleptic malignant syndrome. 6) Heat emergencies. 7) Persistent consciousness disturbance and Brain death. 7-1) Persistent consciousness disturbance. 7-2) Brain death.

**Results:** In 2010, JRC presented JRC resuscitation guideline 2010 based on 2010 Consensus on Science with Treatment Recommendations (CoSTR) by International Liaison Committee on Resuscitation (ILCOR), following American Heart Association (AHA) and European Resuscitation Council (ERC). NR was adapted the original and independent chapter in JRC Guidelines 2010. Main target of NR is on improving acute care of neurological diseases with epidemiological approach.

**Conclusions:** NR guidelines is the first guideline for management of acute stage of neurological diseases. For education of NR, several training courses such as Immediate Stroke Life Support (ISLS), Prehospital Stroke Life Support (PSLS), Primary Neurosurgical Life Support (PNLS) and Advanced Coma Evaluation and Care (ACEC) were developed. 2015 is scheduled as new guideline year by ILCOR. Now, NR is revising and revision process will be completed within 2015.
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