

# HONG KONG MEDICAL JOURNAL

## 香港醫學雜誌

Vol 7 No 4 December 2001

Supplement

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第二屆「世界華人神經病學」學術研討會及第十四屆「香港腦科學會」週年學術會議  
二零零一年十一月九至十二日

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**Intraarterial Thrombolysis and Immerging  
Interventional Strategies for Acute Ischemic Stroke****S1****Lawrence Wechsler***Stroke Institute  
University of Pittsburgh Medical Centre  
Pittsburgh, USA*

Over the past decade, thrombolysis for acute ischemic stroke has progressed from anecdotal case reports and small series to randomized clinical trials. The NINDS tPA trial demonstrated the benefit of intravenous tPA for treatment of stroke within 3 hours of onset. Unfortunately most patients do not reach the emergency department in time for treatment with intravenous tPA. In addition, evidence is accumulating that occlusions of larger arteries such as the middle cerebral artery respond poorly to intravenous tPA.

Direct intra-arterial infusion of thrombolytic agents offers an alternative to intravenous therapy and has several advantages. First, this technique delivers the thrombolytic drug directly to the site of the clot, maximizing concentration within the thrombus and minimizing activation of systemic thrombolysis. This should improve recanalization and hopefully reduce hemorrhagic complications. In addition, the amount of thrombolytic agent given is only enough to clear the clot. If no thrombus is seen, no thrombolysis is needed. The major disadvantage is the need for an interventionalist and the additional time necessary to perform the endovascular procedure.

The PROACT II study was a randomized controlled trial comparing intra-arterial thrombolysis with prourokinase and heparin to heparin treatment alone in patients with stroke due to middle cerebral artery occlusion within 6 hours of onset. One hundred eighty patients were randomized in a 2:1 ratio and followed for 90 days. The primary outcome measure was the percent of patients with modified Rankin scores of 2 or less at 90 days. There was a significant benefit in favor of intra-arterial prourokinase treatment with 40% of patients treated with prourokinase reaching the primary outcome measure and only 25% of controls. ( $p=0.043$ ). All secondary outcomes showed a trend in favor of intra-arterial prourokinase treatment. Recanalization at 2 hours was 66% in the prourokinase group and 19% in controls. Symptomatic hemorrhages at 24 hours occurred in 10% of patients treated with prourokinase and 2% of controls. This study was the first acute stroke trial to show a benefit of therapy as long as 6 hours from stroke onset. In fact, most patients were treated between 5 and 6 hours after stroke.

Despite these promising results, good outcomes were only achieved in 40% of patients and hemorrhages were significantly more common. In most intra-arterial thrombolytic procedures, one to two hours of infusion are needed to lyse clots, particularly large clots in the proximal intracranial arteries. Thus there is much room for improvement. Mechanical devices offer the hope of more rapid thrombolysis and lower hemorrhage rates. Several devices are now being tested for intracranial thrombus removal including catheters using ultrasound, laser technology and high speed saline jets. Phase I clinical trials are now in progress to test the safety and efficacy of these catheters. Other new approaches include combined intravenous and intra-arterial thrombolysis, ultrasound enhanced thrombolysis and improved patient selection using CT and MR imaging techniques.

**Intravenous Thrombolysis with Urokinase for Acute  
Cerebral Infarctions****S1****Qing-tang Chen***Department of Neurology  
Peking University First Hospital  
Beijing, China*

This is a multicenter, randomized, double-blind, placebo controlled clinical study, also the second phase of a 5-year National Project

“A clinical study of the thrombolytic therapy for acute cerebral infarctions within 6 hours from the symptom onset”.

**Objective**

To evaluate the efficacy and safety of urokinase (UK) in the treatment of acute cerebral infarctions within 6 hours from the onset of stroke.

**Patients and Methods**

Patients consistent with the inclusion criteria were randomized into 3 groups. Patients in Group A received UK 1.5 MU intravenous infusion over 30 min, patients in Group B received 1.0 MU of UK intravenous infusion over 30 min, and patients in Group C received placebo (NS) instead of UK. Each patient received a standard therapy after UK or NS: low molecular dextran 500ml intravenous infusion per day for 10 days, and aspirin 300mg, 24h after UK or placebo, per day for 10 days and then 100mg for 80 days (altogether 90 days for aspirin administration). The European Stroke Scale (ESS), Barthel Index (BI) and modified Rankin Scale (mRS) were used to evaluate the recovery of neurological functions.

**Results**

511 patients were enrolled in this study from July, 1998 to December, 2000. The target population was 465 patients because 46 patients did not meet the inclusion criteria. The ESS scores increased rapidly after therapy, especially within the first 24h. The increase of ESS in Group A and B was significantly higher than Group C, and Group A significantly higher than Group B. The stepwise logistic regression analysis revealed if the increase of ESS scores more than 10 points within 24h, the possibility of complete recovery or near complete recovery of neurological functions at the end of 3 months will increase 2 folds. In our study, the non-symptomatic hemorrhagic rate was 9.03% in Group A (14/155), 5.56% in Group B (9/162), and 4.73% in Group C (7/148). No significant difference among 3 groups ( $p=0.284$ ). Symptomatic hemorrhagic rate was 4.52% in Group A (7/155), 3.09% in Group B (5/162), and 2.03% in Group C (3/148). No significant difference among 3 groups ( $p=0.517$ ). The mortality rate was 9.7% in Group A, 1.1% in Group B, and 6.8% in Group C, respectively. 17 cases (3.33%) died of large cerebral infarctions and 8 cases (1.57%) died of cardiac failure. 6 cases (1.89%) (4 in Group A, in Group B and none in Group C) died of symptomatic hemorrhage. No significant difference in mortality rate among 3 groups ( $p=0.294$ ). In BI, 47% of patients in Group A, 44% in Group B, and 38% in Group C got favorable scores (95-100). There was significant difference between Group A+B vs Group C ( $p=0.008$ ), but no difference between Group B and Group C ( $p=0.30$ ). In mRS, 44.9% of patients in group A, 45.51% in Group B, and 31.88% in group C got favorable scores (0-1). There was significant difference between Group A and Group C ( $p=0.020$ ), Group B and Group C ( $p=0.002$ ).

**Conclusion**

We concluded that UK was effective and relatively safe in treatment of acute cerebral infarctions within 6h from the symptom onset.

**Genetics and Strokes****S1****Frank Yatsu***Department of Neurology  
University of Texas – Houston Medical School  
Houston, USA*

Stroke is a generic term for a number of vascular syndromes which affect the brain such as ischemic strokes due to atherosclerosis or to emboli of various causes, aneurysms, intracerebral hemorrhage, arteriovenous malformations, and many others. The most common cause of strokes is the first and because atherosclerosis is recognized to be multifactorial, the genetics of it would similarly be expected to be multiple. Although the known risk factors for atherosclerosis causing strokes and coronary heart disease are similar, such as hypertension, diabetes, smoking, increased cholesterol and a few

other factors such as age, sex, stress, obesity and lack of exercise, the known differential involvement of cardiac versus cerebral vessels with disease and physiological functions suggest that inherent differences in genetic makeup may predispose to stroke.

With the delineation of the human genome and development of microtechnology in which a large number of microanalyses of nucleotides and proteins can be undertaken quickly and accurately, the entire approach to the genomics and proteomics of disease has changed recently. Before this time, single gene or protein analyses were undertaken and correlated with a disease process, but now hundreds or even thousands of these compounds can be analyzed, requiring use of computational strategies or bioinformatics to analyze. Thus the future studies on the genetics & proteomics of strokes will primarily utilize these advanced tools.

In past studies, we studied factors which we believed important in the genetics of strokes due to atherosclerosis and investigated the in vivo dynamic turnover and metabolism of radiolabelled low and high density lipoprotein (LDL & HDL) and found that stroke patients have impaired metabolism which favored an imbalance toward LDL and against HDL, an "atherogenetic profile". Further, to assess the possible genetic basis for this, we investigated gene polymorphisms for LDL, HDL, VLDL and Angiotensin Converting Enzyme (ACE). Interestingly, we found racial differences in that Caucasian strokes subjects showed LDL polymorphism only while African American stroke patients showed significant polymorphism of HDL, VLDL, & ACE as compared to controls.

With the possibility of studying thousands of these potential gene polymorphisms as well as proteins simultaneously using advanced microtechnology, we propose studies on ischemic strokes which will hopefully define a gene expression and proteomics profile which will identify the highly susceptible individuals. At least 5,000 proteins and their corresponding genes have been identified in critical areas for ischemic strokes, and some factors, such as those for hypertension, diabetes, lipid metabolism, and vascular biology will be assayed by their genomic profile while factors which are modified as a "life style" and aging processes will be studied with proteomics. These latter factors include those affecting inflammation, thrombosis, smoking sites, apoptosis, connective tissue, membrane receptors/channels and others.

With a planned study of major stroke centers throughout the world, it is expected that a complex but distinctive gene expression and proteomics profile will emerge which will powerfully predict those individuals who are particularly vulnerable for ischemic strokes. And with a specific profile, as opposed to generic data derived from epidemiological studies, it should be possible to advise patients on what specific interventions will help reduce stroke occurrence. The future potentials for developing a precise gene expression and proteomics profile for ischemic strokes appears very probable.

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## SYMPOSIUM II - UCB SYMPOSIUM ON EPILEPSY

### Advances in the Treatment of Epilepsy

S II

#### Simon Shorvon

National Neuroscience Institute  
Singapore

In this talk, three areas will be covered: (a) advances in the basic understanding of antiepileptic drug action, (b) recent new drugs introduced into clinical practice, and (c) advances in the comparative clinical assessment of antiepileptic drugs. (a) The recent advances in molecular genetics have great potential for the treatment of epilepsy. A much clearer understanding of the mechanisms of action of antiepileptic drugs is possible. Most antiepileptic drugs act on the neuronal sodium channel. The 3D structure of the sodium channel has recently been elucidated as well as its detailed molecular make-up. The effect of drugs on the physiology of the channel, expressed

in *zenopus* oocyte has also been elucidated. It should now be possible to identify what aspects of sodium channel function determine drug effect. Similar advances are being made in respect to the GABA<sub>A</sub> receptor. Recently licensed newer antiepileptics (for instance levetiracetam and topiramate) act by novel mechanisms and thus may have novel clinical properties and these will also be discussed. (b) In the past few years, several new drugs have been introduced into clinical practice which have the potential to improve the therapy of patients with a variety of different forms of epilepsy. These include topiramate, oxcarbazepine and levetiracetam. The specific features of these new drugs will be outlined and their strengths and weaknesses. (c) The comparative clinical assessment of the newer antiepileptic drugs has been stimulated by methods of meta-analysis. The data can be analysed in various novel ways which permit evidence-based comparisons to be made. These methods will be outlined and the results from the meta-analysis of various recent RCTs will be presented.

### MEG in Temporal Lobe Epilepsy

S II

#### Chun-hing Yiu

Division of Epilepsy, The Neurological Institute  
Taipei Veterans General Hospital  
Taipei, Taiwan

The object of this study was to evaluate the orientations and anatomical locations of magnetoencephalographic (MEG) spike dipoles in patients with anterior temporal lobe epilepsy (TLE). With a whole-scalp neuromagnetometer, we measured interictal spikes in 4 patients with medically intractable temporal lobe seizures undergoing presurgical evaluation and subsequently receiving tailored anterior temporal lobectomy. Two types of MEG spike dipoles were identified: anterior horizontal dipoles in three patients and anterior vertical dipoles in one patient. The anatomical location of the epileptiform discharges as determined by MEG was within the resected area in all patients who became seizure-free after surgery with a mean follow-up of 4 months. We preliminarily conclude that the correlation might validate MEG as a noninvasive and practical tool for the evaluation of patients with TLE. Further investigation is required to determine the reliability of the spike dipole localization by MEG in patients with TLE.

### Genetics of Epilepsy: From Bench to Bedside

S II

#### Gardian Fong

Division of Neurology, Department of Medicine  
Queen Mary Hospital  
Hong Kong

Molecular genetic principles and techniques have had a profound impact in the field of neuroscience and epilepsy and in elucidating the molecular and pathophysiologic bases of neurologic disease. The tools of molecular genetic have been used in multidisciplinary approaches to understand the pathogenesis of neurologic diseases. The identification of "disease genes" will have significant consequences for the particular neurological disease involved. Although it is not an instance cure, disease gene identification may have immediate applications in the practice of clinical neurology, for example, enabling presymptomatic and prenatal diagnosis and providing prognostic information.

In general, genetic epilepsies can be divided into a) genetic epilepsies with primary and exclusive symptoms of either generalized (eg benign familial neonatal epilepsies, childhood absence epilepsy and juvenile myoclonic epilepsies) or partial seizure (eg autosomal dominant nocturnal frontal lobe epilepsy); b) genetic epilepsies associated with severe neurologic deficit or malformations (eg cortical dysplasia), or associated with progressive degenerations (eg progressive myoclonic epilepsies); and c) idiopathic epilepsies with generalized seizures suspected of being genetics. About 40% of adults and children with epilepsy have genetic epilepsy with primary generalized seizures. Many of



them are complex genetic diseases that the epilepsy trait can be influenced by many genetic and environmental factors. With the advances in molecular genetic techniques, a number of genetic epilepsies were studied and their chromosomal loci and underlying mutations were identified. This made further understanding of detailed molecular physiology and pathogenesis possible.

In the future, recognition of expression pattern in molecular level may lead to new methods of identifying susceptibility to epilepsies and exposures to noxious agents, improve choice of drug therapy, exercise preventive measures and give accurate prognostic assessment. Nevertheless, a task force for epilepsy classification was set up trying to incorporate the genetic information identified in the last decade.

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## SYMPOSIUM III - STROKE

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### Stem Cell Transplantation for Stroke

S III

**Lawrence Wechsler**

*Stroke Institute  
University of Pittsburgh Medical Centre  
Pittsburgh, USA*

Despite recent advance in stroke prevention and acute stroke treatment there are millions of stroke survivors living with disabilities. At present there is little to offer to improve neurological deficits due to stroke other than physical, occupational and speech therapy. Neuronal transplantation offers the hope of improving neurological function months or years after the recovery process is complete.

Several promising avenues of investigation exist for restoring or augmenting function after stroke. Stem cells may differentiate into functioning neurons, but the fetal origin of such cells limit availability and applicability. Porcine xenografts avoid these problems but may cause rejection or carry foreign viruses. LBS neuronal cells are derived from a cell line originally isolated from a lung metastasis form a testicular germ cell tumor. One clone from this tumor, when exposed to retinoic acid, differentiates into a pure population of neuronal cells. These cells express typical neuronal proteins, form synapses, and extend processes. When implanted in animals the cells survive and integrate with the host. Functional improvement has also been demonstrated in rats following stroke with improvement in both motor and cognitive tasks.

Based upon this promising pre-clinical data, a phase I trial was initiated to examine the feasibility and safety of transplantation of LBS neurons in patients with established motor stroke. Twelve patients were treated with implantation of LBS neurons delivered by stereotactic techniques. Patients were included with stroke involving the basal ganglia. Only stroke between 6 months and 6 years duration were included. Patients were eligible if they had a significant motor deficit that remained unchanged on 2 examinations at least 2 months apart. Pre-operatively patients were evaluated with PET scans, MRI, NIHSS, ESS, Barthel, and SF-36 scales. Post operative neurological assessments were performed at frequent intervals, and PET scans and MRI scans were repeated at 6 and 12 months. Cyclosporin was started one week before surgery and continued for 8 weeks afterwards. The cells were administered using standard stereotactic techniques through a burr hole. The first 4 patients received 2 million cells in one pass. The next 8 patients were randomized to 2 million or 6 million cells in 3 passes.

No surgical or cell related complications occurred during the course of this study. One patient suffered a single seizure 6 months after implantation which has not recurred. Another patient had a brainstem stroke 6 months after the procedure.

Several patients reported subjective improvements in neurological function. This included improved walking, less spasticity, improved strength and memory. In most cases this correlated poorly with the results of stroke scales. Seven of 12 patients showed some improvement in the ESS at 12 months although there were not significant overall changes in the mean NIHSS or ESS. There was a trend towards greater improvement in the patients receiving 6 million cells compared to the 2 million cell group.

However, this study was not designed to test efficacy and in this small group of patients the significance of such findings is limited.

A larger study with controls and larger numbers of cells is currently in progress. Whether these cells or some other cell line ultimately proves useful, neuronal transplantation offers hope for a new era in stroke rehabilitation.

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### Short-term Complications of Carotid Angioplasty and Stenting

S III

**Ping-keung Yip**

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National Taiwan University Hospital  
Taipei, Taiwan*

Contrary to the belief in the past, carotid artery disease is no longer uncommon for the Chinese population living in Taiwan. According to recent hospital-based epidemiological studies in Taiwan, severe (>50%) carotid artery stenosis constituted about 27% of patients experienced transient ischemic attack, 12% of all ischemic stroke and 50% of ischemic stroke due to large artery atherosclerosis.

Besides medical therapy, interventional treatment has been advocated to treat severe carotid stenosis in the past decade. Carotid angioplasty and stenting (CAS) has been a contemporary alternative to carotid endarterectomy. Major concerns of CAS are focused on the effectiveness for stroke prevention and the occurrence of adverse events. Complications of CAS can be classified into 2 types: short-term (acute) and long-term (delayed). The present presentation will focus on the frequencies and risk factors of the short-term complications as review from major series and our own experience from National Taiwan University Hospital.

Short-term complications of CAS can be divided into 3 different categories: (i) mechanical, (ii) angiographic related and (iii) neurological events. Mechanical complications include postprocedural bradycardia (and asystole), hypotension, and hypertension. Postprocedural hypotension and bradycardia may be related to carotid sinus stimulation, both of which are common and almost benign conditions. However, postprocedural hypertension may be related to intracranial hemorrhage that may be fatal. Therefore, it is necessary to monitor postprocedural hemodynamic condition and may be mandatory to treat markedly elevated blood pressure to prevent secondary neurological complications. Intimal dissection, aneurysm formations, arterial spasm, plaque rupture, vessel rupture and balloon rupture are encountered less frequently. Groin hematoma, femoral artery aneurysm and arterio-venous fistula are considered as complications that are related to angiographic procedure but not to CAS. Neurological complications may occur during or after procedure. Hemodynamic cerebral ischemia may occur during balloon inflation and is also noted during antihypertensive treatment after CAS. Cerebral embolism may occur during endovascular manipulation. Hyperperfusion syndrome due to compromised cerebral autoregulation has also been reported. Herein, we will present the frequencies of these short-term complications, possible risk factors of their occurrence, clinical and radiological manifestations of these neurological complications.

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### Low-molecular-weight Heparin for the Treatment of Acute Ischemic Stroke: A Randomized Controlled Trial

S III

**Chuan-zhen Lu**

*Institute of Neurology, Department of Neurology  
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#### Objectives

Anticoagulation with unfractionated heparin is used commonly for treatment of acute ischemic stroke, but its use remains controversial

because it has not been shown to be effective or safe. Low molecular weight heparin (LMWH) have been shown to be effective in preventing deep vein thrombosis in the patients with stroke. This trial of acute stroke treatment in Shanghai will investigate the efficacy and safety of LMWH in acute ischemic stroke patients.

## Methods

Our trial was a multi-centre, randomized, add on, controlled on the effect of LMWH for treatment of 856 patients with acute ischemic stroke. 443 Patients were randomly assigned within 48 hours of the onset of symptoms to receive LMWH (Fraxiparine, 4100 anti-factor Xa IU twice a day) subcutaneously for 10 days and 413 patients to receive routine method (dextran 500 ml and radices salviae miltiorrhizae 24g once daily) intravenously for 10 days as the control group. The measure of outcome was the grade of Chinese stroke scale and activities of daily living at 10 days, 21 days and 3 months.

## Results

There are no difference in the ratio of sex, the scale of anamnesis, concomitant, and initial Chinese stroke scale between the LMWH and control group ( $p>0.05$ ). The age of the LMWH group was young than the control group ( $p<0.05$ ). We found the significant difference of the Chinese stroke scale after treatment 10 days and 21 days between the LMWH and control group ( $p<0.01$ ,  $p<0.05$  respectively), but there were no significant difference of the ADL after 21 days and 3 months in two groups ( $p>0.05$ ). During the treatment, the bleeding events in LMWH group was 5.87% more than the control 1.69% ( $p<0.01$ ). The death was no significant difference in two groups after treatment 21 days and 3 months.

## Conclusions

Despite an apparent positive response to treatment at 21 days, but LMWH for acute ischemic stroke within 48 hours of the onset of symptoms is no associated with an improvement in ADL at 3 months.

## Use of Statin for Regression of Cerebral Artery Stenosis (ROCAS): A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study

S III

**Ka-sing Wong**

*Department of Medicine & Therapeutics  
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Hong Kong SAR*

## Background

The use of statin to prevent stroke has attracted a lot of interest but its pathophysiological basis has been lacking. There has been no report of randomized study on the use of statin for regression of hemodynamically significant arterial stenosis in the cervico-cranial circulation.

## Methods

The aim of ROCAS is to investigate the effect of statin of the progression of cerebral artery atherosclerosis. We screened asymptomatic subjects with risk factors for intracranial atherosclerosis (such as hypertension and diabetes) with transcranial Doppler for middle cerebral artery stenosis and confirmed the diagnosis by magnetic resonance angiogram (MRA). Normal to mildly hypercholesterolaemic subjects (fasting LDL-cholesterol between 3.0 - 5.0 mmol/L) were assigned to simvastatin 20 mg or placebo daily. The primary measure of outcome is the change of middle cerebral artery stenosis as measured by MRA, which were performed at baseline and after 2 years on treatment, using a computer-assisted measurement of the percentage stenosis. Secondary measures of outcome included progression or regression as judged by the panel-reading method as used in the MARS study; changes in the smallest cross sectional area of the M1 section of middle cerebral artery as appear on the MRI; changes in the peak systolic velocity of middle cerebral artery in transcranial Doppler; clinical events: stroke, transient ischemic attacks, acute myocardial infarction, sudden death and any mortality.

## Results

From August 1996 to June 1999, we screened 3,882 patients and randomized 227 patients. There were 153 women (67%) and the average age was 61 (36-75). Average LDL-cholesterol level was 3.93 mmol/L (3-5). The last angiographic study will be completed in May 2001 and final results will be presented.

## SYMPOSIUM IV - EPILEPSY

### Epidemiology of Epilepsy

S IV

**Simon Shorvon**

*National Neuroscience Institute  
Singapore*

This lecture will be divided into three parts. (a) The burden of epilepsy has now been studied in many countries. The data suggests that in most areas of the world epilepsy is common and has similar features. Various data will be presented from recent studies in the UK and elsewhere which have attempted to quantify the burden of both newly diagnosed and also chronic epilepsy. The genetic differences between populations and the extent to which these underpin epidemiological differences in the phenotypic expression of epilepsy are areas of active study and will also be discussed. (b) The mortality of epilepsy has been the subject of recent emphasis. The epidemiological and clinical features of sudden unexplained death in epilepsy (SUDEP) have been the focus for these studies, and these will be reviewed. Epidemiological studies have pointed to possible mechanisms of SUDEP and the potential for prevention. (c) Recent population based surveys of treatment and prognosis have been carried out, which help define the role and impact of therapy. Two recent studies from the UK will be discussed, which have taken the form of population-based longitudinal cohort studies and show that the early course of the epilepsy and response to treatment are important predictors of overall prognosis. It is now also apparent that the potential for therapy is not fully exploited in many patients but also in patients with chronic epilepsy, altering antiepileptic drug therapy is often ineffective. The patterns of treatment in these population studies will be discussed.

### Epileptology in Mainland of China

S IV

**Xun Wu**

*Department of Neurology  
Peking University First Hospital  
Beijing, China*

Epilepsy is common, especially in childhood. In mainland of China the lifetime prevalence is 4.4/1000, incidence is 35/100,000/y, mortality is 9/100,000, and remission rate is 70%~80%.

Prior to the 1970's, the Epilepsy Team, Chinese Society of Neurology and Beijing League against Epilepsy were founded. Until today, The Epilepsy Center was established in Beijing, Shanghai, Guangzhou, Chongqing and Chengdu. In additionally, Epilepsy Clinics were founded in several Medical College.

The first line antiepileptic drugs such as phenobarbital, phenytoin, primidone, benzodiazepine, carbamazepine and valproate were used to therapy. From 1990's some new antiepileptic drugs were marketed, including topiramate and lamotrigine.

Presurgical evaluation of epilepsy, surgical candidates must have the following localization methods: video-EEG, Wada test, neuro imaging (CT, MRI, MRS, SPECT and/or PET), some times including CoEEG, epidural electrode and intracerebral electrode EEG. According to the localization, the following surgical procedures were selected: anterior temporal lobectomy, amgdalohippocampectomy, lesionectomy, corpus callosotomy, hemispherectomy, multiple subpial transection and vagus nerve stimulation.

The study of mechanism of epilepsy involved molecular biology, neurotransmitter, neuro-biochemistry and neuropathology.

## Neuropsychological Effects of Epilepsy and Antiepileptic Drugs

STV

**Patrick Kwan**

Patients with epilepsy are recognised to have a higher prevalence of cognitive and behavioural dysfunction than the general population. This is the result of complex interactions among a number of multifaceted and overlapping factors including the underlying neuropathologies, ictal and interictal neuronal discharges, a plethora of antiepileptic drugs, and numerous psychosocial issues. Research into the clinical relevance of these factors has been dogged by a range of methodological pitfalls, mainly reflecting lack of standardisation of the neuropsychological battery, small numbers of study subjects and multiple testing, and statistical failure to appreciate the differential effects of these interactive elements in individual patients. Although antiepileptic drugs can impair neuropsychological functioning, their positive effect on seizure control may in turn improve cognition and behaviour. Each person should be assessed individually with regard to the factors unique to the seizure disorder and its treatment in order to gauge their potential adverse effects on the person's cognition and behaviour.

## SYMPOSIUM V - NEUROMUSCULAR

### Pathogenesis and Treatment of Inflammatory Neuropathy

SV

**Richard Hughes**

Department of Neuroimmunology  
University of London  
London, United Kingdom

#### Introduction

This lecture will focus on the autoimmune inflammatory neuropathies Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). GBS is now recognised to have three different pathological substrates, acute inflammatory demyelinating polyradiculoneuropathy (AIDP), which accounts for 95% of cases in Europe and north America, acute motor axonal neuropathy (AMAN), which has been most commonly reported from northern China, and acute motor and sensory axonal neuropathy (AMSAN).<sup>1</sup> There are variant or related conditions of which the Fisher syndrome of ophthalmoplegia, ataxia and tendon areflexia is the most common. CIDP is usually a relapsing and remitting or progressive sensory and motor disorder but predominantly sensory and predominantly motor forms occur. Multifocal motor neuropathy (MMN) has been distinguished as a related but separate condition.

#### Causes

*Campylobacter jejuni* infection is responsible for about 25% of cases of GBS in European and North American serological studies and is also the commonest identified cause in other parts of the world including China and Japan. The strains of *C jejuni* responsible for GBS tend to be rare strains which are not common causes of enteritis. Other causes of GBS are cytomegalovirus, *Mycoplasma pneumoniae* and probably Epstein-Barr virus and *Haemophilus influenzae*. There must also be a host factor involved in the pathogenesis since in an outbreak of *C jejuni* enteritis only about 1 in 1000 develop GBS. The nature of the host factor is not clear. It is likely to be an immune susceptibility gene. The MHC class II gene, HLA DBQ1\*03, was more common in GBS due to *C jejuni* than in GBS due to other causes.<sup>1</sup>

#### Gangliosides

Antibodies to gangliosides are found in the serum of many patients with acute inflammatory neuropathy. In Fisher syndrome

IgG antibodies to GQ1b are present in almost all cases. GQ1b is more abundant in the ocular motor nerves and is present on a subset of dorsal root ganglion cells. Antibodies to GQ1b stain terminal motor axons and block conduction in a mouse phrenic nerve diaphragm model.<sup>2</sup> The bacterial wall of *C jejuni* contains a glycoconjugate which mimics the GQ1b epitope in myelin and may stimulate an antibody response which cross-reacts with the ganglioside. In AMAN IgG antibodies to GM1, GM1b, GD1a, and N-acetylgalactosaminyl GD1a are all found. A monoclonal antibody to GD1a stains motor and not sensory axons. Antibodies against GD1a or another ganglioside located on motor axons would explain the pathogenesis of AMAN. Antibodies to gangliosides are less common in CIDP. IgM antibodies to GM1 are present in the serum of about half of all patients with MMN but have not been shown to be involved in pathogenesis or predictive of response to treatment.<sup>1</sup>

#### Proteins

Immunising rats with any of the myelin proteins P2, P0 or PMP22 produces experimental autoimmune neuritis, an accurate model of the common AIDP form of GBS. This is primarily a T cell disease since it can be transferred with T cells alone. The model suggests that loss of tolerance to peripheral nerve myelin proteins causes AIDP. There is limited evidence for immune responses to these proteins in GBS.<sup>1</sup> Recently Pollard and colleagues have shown that IgG antibodies to P0 are present in about 25% of CIDP patients and will cause demyelination upon injection into rat sciatic nerves.<sup>3</sup>

#### Treatment

Steroid treatment is beneficial in CIDP<sup>4</sup> but surprisingly not in GBS<sup>5</sup> and it may make MMN worse. The lack of efficacy might be due to an adverse effect of steroids on denervated muscle. Plasma exchange has been shown in randomised controlled trials to be effective in GBS<sup>6</sup> and CIDP. There is inadequate evidence to say whether it is effective Fisher syndrome or MMN. Intravenous immunoglobulin (IVIg) has been shown to be equivalent to plasma exchange in four randomised controlled trials in severe GBS during the first two weeks of the disease.<sup>7</sup> It has become the treatment of choice because of its greater convenience. In MMN IVIg is certainly the treatment of choice, being the only treatment to have been shown to be effective in randomised controlled trials.<sup>8</sup> In CIDP IVIg has been shown to be beneficial in randomised controlled trials but steroids are preferred because of their convenience and lesser cost.<sup>9</sup> Immunosuppressive drugs are commonly used in CIDP and MMN but there are no adequate trials to support their use.

In GBS excellent intensive care is the basis of good practice and needs to include monitoring vital capacity, respiratory care, ECG monitoring and prophylaxis for deep vein thrombosis.<sup>10</sup> Prescriptions for pain control require care because of autonomic instability. In all forms of inflammatory neuropathy there is a risk of persistent disability and fatigue is common. A multidisciplinary approach to management is important and in Europe and the USA lay organisations have been helpful in providing patient support. The web site for the GBS Foundation International is [www.webmast.com/gbs](http://www.webmast.com/gbs) and for the GBS Support Group [www.gbs.org.uk](http://www.gbs.org.uk).

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## Clinical Observation of Myasthenia Gravis in Taiwan

SV

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For the last 2 decades, we collected 1355 patients with myasthenia gravis (MG) in Taiwan. There were 488 males and 867 females. Three hundred and twenty patients (23.6%) had disease onset before puberty (Age <16), and 1035 (76.4%) had onset after puberty (Age >16). Restricted ocular MG was encountered in 51.8% of all MG patients and account for 75% of these with juvenile. Autoimmune thyroid diseases (Grave's disease) occurred in 10% of all patients, other autoimmune associate diseases were: vertigo, systemic lupus erythematosus, rheumatoid arthritis and idiopathic thrombocytopenic purpura. The titer of anti-acetylcholine receptor antibody (anti-AchRab) was measured using a radioimmunoassay by RSR AchRab Kit (RSR Limited, Cardiff, UK). Anti-AchRab titer in untreated MG patients showed considerable variation from 0-3500nmole/l. The antibody negative (<0.2nmole/l) encounter 24.3% of all MG patients, 27.2% in juvenile MG and 24.4% in adult MG. The positive anti-AchRab titer (>0.2nmole/l) was 58% in ocular MG and 91% in generalized MG. Three hundred and ninety-five cases had thymectomy or thymomectomy. The findings of thymic pathology were thymoma in 117 (29.6%), hyperplasia in 228 (57.7%), atrophy thymus in 45 (11.4%). Symptomatic treatment only in 12% of patients, most of cases (88%) had either or thymomectomy thymectomy or with immune therapy. Plasmapheresis (PP) has been shown to be a successful therapy for patients with MG crisis or fulminant progression. A total of 146 patients (10.8%) received PP therapy, all patients tolerated PP well, although 2.3% of them experienced hypotension. Both double filtration (DF) and immunoabsorption (IA) methods effectively ameliorate symptom and signs of MG. IA removed AchRab more effectively than DF does, but clinical effective between these 2 methods are similar, a daily schedule seems more effective than an alternate daily schedule. The optimal number of PP sessions for each course is 4. Seven patients with advanced MG who were refractory to thymectomy and immunosuppressants received daily 0.4g/kg doses of intravenous immunoglobulin G (IVIG) for 5 consecutive days. IVIG therapy is an effective and safe treatment for refractory MG.

## Current Overviews of Neuromuscular Diseases in China

SV

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Recently, molecular study in NMD has been performed in different fields. Here we introduce some works as follows: Muscular Dystrophy DMD/BMD Dystrophin gene mutation can be detected in

more than 10 hospitals in some areas in China using either Southern blot analysis or multiple PCR of 9 to 18 pair exons in hot spots. Gene deletion were found in about 49.3% (among 340 cases) to 59% of DMD and BMD cases by using mPCR. Carrier detection and prenatal diagnosis has been started. 27 family has been analyzed by using quantitative analysis and Short Tandem Repeat sequence (STRs-PCR) linkage analysis. 7 obligated carriers were correctly confirmed and 11 females were diagnosed as gene deletion carrier among 21 possible carriers assessed by family linkage analysis. LGMD Five cases of sarcoglycanopathy has been identified among 25 cases of autosomal recessive LGMD by using  $\alpha$ ,  $\beta$ ,  $\gamma$ ,  $\delta$ -sarcoglycan immunostaining and immunoblotting procedure, among which two were LGMD2D( $\alpha$ -SG), another two were 2F( $\delta$ -SG) and the last was 2C( $\gamma$ -SG). No case of sarcoglycanopathy was found in this group. FSH Genotype analysis by using the p<sup>13E11</sup> probe is still studying in 26 FSH patients. EcoR1-BlnI double digestion was routinely used to avoid the interference of small EcoR1 fragments of 10qter origin. The 4q35 EcoR I fragment of 20 FSH cases out of 26 cases were smaller than 38kb. Distal Myopathy 46 cases of distal myopathy has been reported in which there was no autosomal dominant type. The clinical and histochemical findings were coincided with Nonaka and Miyoshi type in 40, Welander-like type in 3, TMD-like in 2, OPDM in 1 case. Mitochondrial myopathy and encephalomyopathy 75 cases of mitochondrial myopathy and encephalomyopathy had been studied using molecular studies of skeletal muscle mtDNA 24 cases were identified with mtDNA mutation, including 6 large scale deletion(3 KSS,3CPEO), 11 A3243G point mutation(10 Melas,1KSS), 4 A8344G point mutation (2 MERRF,2 LS) 11 A3243G point mutation ( 10 MELAS,1KSS),4 A8344G point mutation(2 MERRF,2LS), 1 T8993G (1 LS), T8993C (1 LS).1 A molecular analysis of peripheral blood mtDNA was also studied. Lipid Storage Myopathy and Other More than 100 cases of lipid storage diseases have been found in China which were confirmed by histochemistry and EM study. The reason of high frequency of this kind of disease in china remains uncertain. 10 cases of acid maltase deficiency have been reported.Spinal Muscular Atrophy (SMA) DNA genetic study has been performed in 195 cases of SMA in three centers. The total rate of deletion of SMN gene in exon 7,8 was detected in 96.4% cases.Charcot Marrie Tooth (CMT) 37 cases of CMT1 patients from 34 unrelated families and 21 cases of asymptomatic members were studied. 67.6% (23/34) of CMT1 patients were identified to have duplications using both restriction analysis of PCR product and STR methods. And the recombination hotspot in Chinese patients was in 1.7kb regions. We have found one patient with connexin 32 gene mutation using single-strand conformational polymorphisms and direct sequencing method in 5 cases of CMTX without CMT1 duplications, it was proved that was G→A transition at point 62, which predicts glycine to aspartate substitution at amino acid 21(G21D). We detected the same region in 50 healthy controls and did not found the same change. It was not reported in the literature that the disease might be caused by the mutation.

## DISAERTATION HIGHLIGHTS

### P-glycoprotein and Multidrug Resistance (MDR) Gene Expression in Epilepsy

DH

**Patrick Kwan**

#### Background

Hippocampal sclerosis (HS) is one of the commonest aetiologies of drug-resistant epilepsy. Over-expression of the drug transporter P-glycoprotein (P-gp) confers chemoresistance in certain cancers. P-gp extrudes a wide range of xenobiotics out of cells and is present in cerebral capillaries where it contributes to the integrity of the blood-brain barrier. It is encoded by the *MDR1* gene in man and the *mdr1a* and *1b* isoforms in rodents. It was hypothesised that over-expression of the *MDR* gene may play a role in the pathophysiology of refractory epilepsy by limiting antiepileptic drug (AED) access to the epileptic focus.

## Methods

A range of single-dose AEDs were administered to *mdr1a* knockout mice, which lack cerebrovascular P-gp, and their brain levels measured. Regional P-gp expression was determined in the normal rat brain by measuring *mdr1* mRNA concentrations. The effects of experimental seizures on the expression of *mdr1* were determined in the brains of genetically epilepsy-prone rats (GEPRs). Temporal lobe tissues resected from patients with refractory epilepsy due to HS were examined for the extent of *MDR1* gene expression.

## Results

Phenytoin, carbamazepine and topiramate reached higher levels in the brains of *mdr1a* knock-out mice than in wild-type mice ( $p < 0.05$ ), suggesting they are substrates for P-gp. The hippocampus of rats expressed both *mdr1* isoforms, while other brain regions expressed *mdr1a* only. *Mdr1a* expression in the midbrain and cortex was higher in GEPRs subject to an audiogenic seizure compared with unstimulated, seizure-free controls. Significant *MDR1* expression was observed in resected tissues from patients with HS.

## Conclusion

*MDR* gene expression may be relevant to the pharmacoresistance of HS. This mechanism may also play a role in other aetiologies of refractory epilepsy.

## Deep Brain Stimulation for Management of Parkinson's Disease

DH

Vincent CT Mok

### Abstract

Deep brain stimulation (DBS) has emerged to be an effective therapy for Parkinson's disease (PD) over the last 10 years. Its origin stems from Hassler's observation during thalamotomies in the 1950s that electrical stimulation of the ventral lateral thalamus could suppress parkinsonian tremor. Advent of oral levodopa in late 1960s led to a decline in surgical treatments during 1970s and 1980s.

Development of DBS came about in the 1990s because of the motor complications associated with levodopa treatments, better neurosurgical technique, better understanding on the pathophysiology of PD and the complications associated with bilateral ablative surgery.

Clinical studies had shown that ventral intermediate (VIM) thalamic stimulation suppresses only contralateral tremor, while subthalamic (STN) stimulation improves all cardinal features of PD. Effects of globus pallidus internus (GPi) stimulation varies with site of stimulation within the GPi. Stimulating ventro-medial GPi suppresses on-dyskinesia while stimulating dorso-lateral GPi improves parkinsonism. Current hypothesis on the mechanism of DBS at a cellular level suggested that high frequency electrical stimulation inhibits neuronal firing via activation of inhibitory GABAergic fibres. The anti-parkinsonian effect of inhibiting STN or GPi can be explained by the current pathophysiological model of PD, which suggests that abnormal firing STN and GPi nuclei contribute to the motor problems of PD.

The success of surgical procedure depends on accurate implantation of stimulating electrode into the targets. This is achieved by image guided stereotactic technique, microelectrode recording and macrostimulation. The principle of postoperative programming is to select the combination of electrical parameters that provide maximal benefit with minimal battery requirement and minimal side effects. Serious adverse events including major intracranial hemorrhage or dementia are in the order of 1%. We performed DBS between 1997 to 2001 on 13 Chinese patients with PD (2 VIM thalamic, 10 STN & 1 ventro-medial GPi) and effects were similar to those reported in published series. There was one major intracerebral hemorrhage induced during implantation of testing electrode. Side effects to the stimulation were mild and reversible.

## SYMPOSIUM VI - PFIZER SYMPOSIUM ON PAIN

### Management of Neuropathic Pain: The Role of Antiepileptic Drugs

SVI

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Clinical trials have demonstrated efficacy of several antiepileptic drugs (AEDs) in the treatment of neuropathic pains, such as painful diabetic neuropathy and trigeminal neuralgia. These and other painful conditions are characterized by high frequency firing along selectively activated neural networks that signal location and intensity of nociceptive inputs. The first neuron in the network is in the periphery, but there also are central components of the circuitry. Thus, potential mechanisms for reducing pain must be sought throughout the circuit. Chronic neuropathic pain may be spontaneous in the absence of stimulation because neurons in the network are hyperexcitable due to several factors. For example, neurons may exhibit pacemaker-like activity as a result of injury or sprouting. Sensitization of peripheral and/or central neurons, resulting in an exaggerated response to stimuli, may occur also. The conundrum of *anesthesia dolorosa*, pain in the absence of sensation to one or more modalities, seems to result from remodeling in the dorsal horn, a process reminiscent of kindling epileptogenesis.

Inappropriate hyperexcitability along the pain processing network spreads from the generator site(s) to the thalamus and cortex. Association pathways from primary sensory cortex to orbitofrontal and cingulate cortex and interconnectivity with limbic structures generate the suffering component of pain and pain behaviors. Mood stabilization can contribute importantly to the management of pain. Pain also may disturb sleep. Improved sleep is another goal of pain management that may increase tolerability of pain. Some AEDs may be useful for treatment of pain because they disrupt the pattern of sustained action potential firing. These pathways overlap the processing pathways of epilepsy and anxiety and share ion channels and neurotransmitters that are molecular targets for AEDs. To the extent these pathways and targets overlap, one would expect AEDs to be useful for the treatment of pain.

There is a longstanding precedent for the treatment of neuropathic pains with AEDs, starting with carbamazepine. Carbamazepine was developed to treat trigeminal neuralgia. It has multiple actions that could contribute to its broad utility. It blocks voltage-sensitive sodium channels in such a way that sustained action potential firing encoding pain is disrupted. It is also an NMDA channel blocker and thus may reduce sensitization, for example. It also increases interstitial serotonin that may activate interneurons to release GABA. Increased serotonin is likely to improve mood and sleep also. These actions make carbamazepine an analgesic, mood stabilizing, antiepileptic drug.

Valproic acid (VPA) was found to have antiepileptic properties before more recent approval for the treatment of bipolar disorder and migraine. Use for the treatment of neuropathic pains is uncommon. VPA is a broad spectrum AED with several identified cellular actions. It increases GABA, blocks sodium current and blocks T-calcium current implicated in absence seizures. High concentrations of VPA increase hyperpolarizing potassium currents. Lithium and VPA, but not carbamazepine, share the ability to block protein kinase C in frontal and hippocampal cortex and decrease G-protein activity. This could prevent phosphorylation of NMDA receptors involved in kindling and cell remodeling that results in chronic pain.

Of the new antiepileptic drugs, most is known mechanistically about gabapentin (GBP). It increases brain GABA content and augments GABA release by a non-vesicular mechanism. The GBP binding site is the  $\alpha_2\delta$  auxiliary subunit of

voltage-sensitive calcium channels. GBP also limits high frequency action potential firing by unknown mechanisms and raises plasma, and presumably brain, serotonin concentrations. This could account for improved stage III and IV sleep in patients taking GBP. There are multiple reports that GBP decreases release of multiple transmitters, including glutamate, substance P, norepinephrine and dopamine.

Lamotrigine is a broad spectrum antiepileptic drug with increasingly recognized analgesic and mood stabilizing effects. It is a use-dependent sodium channel blocker. It blocks N-type calcium channels involved in neurotransmitter release and seems to reduce release of glutamate more than other neurotransmitters. It also has been reported to reduce the synthesis of dopamine by inhibiting tyrosine hydroxylase, an action that could contribute to antipsychotic efficacy.

Topiramate is a fructopyranose compound with broad spectrum antiepileptic activity. Anecdotally, it has efficacy in the treatment of migraine and neuropathic pain. There are also reports of treatment of mood disorders. Topiramate blocks kainate responses, enhances GABA-activated chloride conductance and blocks voltage-sensitive sodium and L-calcium channels.

Newer drugs with the potential for broad clinical utility are emerging. Oxcarbazepine differs subtly from its parent compound carbamazepine by blocking N-calcium channels rather than L-type channels. Its clinical applications overlap those of carbamazepine. Levetiracetam (LVT) was discovered with the kindling model. There is emerging evidence of its multiple uses. Its mechanisms of action are under study. Zonisamide (ZSM) has multiple cellular actions and anti-oxidant properties. By way of speculation, LVT and ZSM may protect against neuronal damage that result in central remodeling and chronic pain.

In summary, new and standard AEDs have been used to treat neuropathic pain. Multiple mechanisms of action have been demonstrated for most of these AEDs. These drugs are tolerable because brain activity is modulated, rather than multiplied or deleted, implying that effects of an AED on its multiple targets are weak or partial. This polypharmacology increases the likelihood of affecting one or more pain-producing neural functions. However, the existence of multiple mechanisms of action is not a guarantee that all patients with a given condition will benefit from a given AED, and not all who benefit will obtain complete relief. In part, incomplete benefit reflects limiting side effects as drug actions exceed tolerable levels at high concentrations. The increasing use of AEDs in the treatment of neuropathic pain is due not to efficacy, however modest, but also because of their safety and tolerability.

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## SYMPOSIUM VII - DEMENTIA

### Dementia in Taiwan

SVII

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Recent advances in dementia during the past decade have identified risk, protective factors, and the pathogenesis of various types of dementia, which lead to several kinds of promising treatment in dementias. As in Japan, the most frequently encountered dementia in the hospitals of Taiwan was reported to be VaD, accounting for 40%, followed by AD for 30%. This was ever explained as the high prevalence of stroke in Taiwan. However, the low percentage of mild dementia (20%) among AD in the hospital subjects raised the possibility of under-reported in AD. Owing to the maturing of longitudinal studies with more consistent and elaborate methods in diagnosing dementia, the prevalence and incidence of dementia have been reinvestigated lately in several large-scaled international collaborating studies. The prevalence of dementia among the people aged 65 and above was around 3-4% and the leading cause of dementia was Alzheimer's disease (AD) accounting for 50-55%, followed by vascular dementia (VaD) for 25-30% and mixed dementia for 15%. The incidence of dementia was about 12-14% per thousand per year and AD was still the leading cause, accounting for about 40%, followed by VaD for 30%. The mortality was very high, 50% for all types of dementia and 70% for VaD in two years. The low prevalence of dementia in the developing countries may result from younger in aged population, higher mortality of demented people and lower diagnostic rate.

Age is the single most important factor for dementia of all kinds, including AD. AD rose between the ages of 65 and 95 years doubling with every 5 years of age as most of western countries. Family history, lack of education, female sex, history of severe head injury, carrying ApoE gene and perhaps vascular risk are reported to be risk factors for AD. Putative protective factors for AD under intense investigation include the use of estrogen in postmenopausal women, NSAIDs, and antioxidant therapies. The low prevalence and incidence of AD in Taiwan might result from low ApoE4 and protection of the family. The risk for developing dementia is seven to ten times among the stroke elderly compared to the non-stroke elderly. The post-stroke dementia is multifactorial, including brain damage from stroke (true VAD), concomitant with AD, AD alone, and systemic causes.

### Dementia in Singapore

SVII

#### Christopher Chen Li-Hsian

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Singapore is a small multi-racial, multi-cultural nation which has undergone tremendous social and economic transformation in the 4 decades since independence – an experience shared with many other Asian nations. Rising standards of living, higher standards of education, good housing, safe water supply and sanitation, a high level of medical services and the active promotion of preventive medicine, have all helped to significantly boost the health of Singaporeans. However, as with many other developing societies in the Asia-Pacific region, this has led to a population age structure that is rapidly maturing: the 11% of the population which is now above 60 years of age is projected to increase to 27% by the year 2030. Changing demographic patterns, alterations in social structures and improvements in healthcare will likely lead to an increase in the prevalence of dementia in Singapore.

In 2000, Chinese formed 76.8% of the population with Malays constituting 13.9% and Indians 7.9% respectively. Community based studies performed in 1985 and 1990 showed that the

prevalence of dementia in elderly Singaporeans was approximately 2% in Chinese and 4% in Malays (no information is available for Indians). By contrast, the prevalence of dementia in Europe and the United States ranges from 3.5% to 14.9%. A low prevalence of dementia (1.8 - 4.6%) has been demonstrated in many studies of Chinese populations.

However, a more recent study of elderly Chinese in Hong Kong, which has an urban environment similar to Singapore, showed that the prevalence of dementia was 6.1%. Using conservative estimates, the number of the demented elderly is anticipated to triple from 7,000 in 2000 to 24,000 in 2030. Further epidemiological studies are being conducted in Singapore using locally validated criteria and studies are under the aegis of the 10/66 Dementia Research Group are being planned.

An increasing number of multi-disciplinary teams for the medical as well as psychological assessment of dementia exist in a number of hospitals. The National Neuroscience Institute's Dementia Programme aims to stimulate higher quality research and training.

Under the aegis of the Ministry of Health and the National Neuroscience Committee, Guidelines for the Management of Dementia were developed and launched for the use of all healthcare professionals in 2001.

## Prevalence of Dementia and Major Subtypes in Four Cities of Northern and Southern China

SVII

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### Background

A lower prevalence of dementia and conflicting findings on the relative frequency of Alzheimer's dementia (AD) and vascular dementia (VaD) have been reported for Chinese populations, but it is unclear whether this observation reflects a low disease risk or an artifact of case finding.

### Objective

To investigate prevalence and epidemiological pattern of dementia and major subtypes in the elderly residents of northern (Beijing, Xian) and southern (Shanghai, Chengdu) China.

### Design

A door-to-door three-phase procedure was used to ascertain dementia. In phase I, a Chinese version of Mini-Mental State Examination was administered to all participants in 1997. In phase II, those who failed the screening tests and those who past in the tests, but having a suspected history of cognitive impairment underwent detailed diagnostic assessment of dementia, AD and VaD using the DSM-IV, NINCDS-ADRDA, and NINCDS-AIREN criteria. In phase III, validity of the diagnostic approach was confirmed by a follow-up study in 1998.

### Participants

A total of 39 474 residents aged 55 years and over from 76 urban and 106 rural communities in four cities of China was drawn through a stratified multiple stage cluster sampling. 37 461 (94.9%) were interviewed.

### Results

A total of 1 283 cases of dementia (63.1% of cases for AD, and 26.8% for VaD) were identified. Age-standardized prevalence in persons aged 55+ was 2.8% for overall dementia, 1.7% for AD, and 0.8% for VaD. The prevalence of AD increased rapidly with age from 0.1% among those aged 55-59 to 30.1% at age 90+.

The prevalence of VaD increased from 0.6% in age 55-59 to 2.1% at age 80-84, then turned down. A difference in

prevalence of AD between women and men was age dependent, although the age-standardized prevalence of AD for women was significantly higher than that for men, i.e., 2.1% versus 1.2%. Nevertheless, the age-standardized prevalence of VaD for women was preceded by that for men, but not significant (0.7% Versus. 1.0%). Variation between northern and southern was great for VaD prevalence, and less for AD prevalence.

The difference in age-standardized prevalence of AD between urban and rural was not significant that was 1.9% versus 2.3% in northern, and 1.3% versus 1.8% in southern. The age-standardized prevalence of VaD in rural communities (1.7%) was significantly higher than that in urban communities (1.0%) in northern; however, the figure (0.3%) in rural was not higher than that (0.6%) in urban in southern. There were no significantly associated between lower education attainment and higher age- and sex-standardized prevalence rates for AD and VaD either in urban or rural area of northern and southern China.

### Conclusion

Our overall prevalence of dementia and its subtypes is considerably higher than previously reported estimates from China and similar to those reported in whites. Compared to VaD, AD was more prevalent in China, either in northern or in southern, in urban or in rural, in men or in women. The overall similarity for AD in both the prevalence estimates and age, gender patterns across regions suggests that limited variation of main risk factors related to AD present worldwide. We did not find evidences to support that lower education and rural setting are independent risk factors for AD.

## Advances in the Treatment of Alzheimer's Disease

SVII

**Jacques Hugon**

Alzheimer's disease (AD) is clinically characterized by the progressive onset of memory disturbances and followed by cognitive impairments including aphasia, apraxia and agnosia. The neuropathological hallmarks of the disease comprised the senile plaques formed by the accumulation of the  $\beta$ -amyloid peptide, by the neurofibrillary tangles mainly composed of abnormally phosphorylated tau protein and by neuronal loss. Sporadic and familial forms of AD are described. The familial cases are linked to gene mutations concerning APP, P51, PS2 genes.

So far, no curative treatment exists for AD. In the past several years, cholinesterase inhibitors have been developed in the treatment of AD in order to increase the level of acetylcholine in the brain. They include tacrine, rivastigmine, donepezil, galantamine and some others. Although the pharmacological benefits are rather modest, patients show a clear cognitive improvement lasting at least for several months. Several other therapeutic targets have been proposed recently according to different aspects of the putative pathogenesis of AD. The amyloid hypothesis has lead the researcher to try to reduce the production of the  $\beta$ -amyloid peptide by inhibiting the  $\beta$  and gamma secretases involved in APP cleavage.

On the other hand, vaccination against the  $\beta$ -amyloid peptide seems to be a promising approach in experimental animals. Reducing inflammation and the production of free radicals are also possible targets now explored. The manipulation of tau phosphorylation, ApoE metabolism and the blockade of neuronal apoptosis are new intriguing and putative targets that are currently analyzed. Finally, as for many other neurodegenerative diseases, stem cell replacement therapy and gene therapy are also envisaged at the experimental level.

In the future combined therapy using different pharmacological approaches in the same patient will probably be needed to attenuate or to block the relentless evolution of the disease.

## Hemodynamic Changes After Carotid Stenting

SVIII

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To study the hemodynamic changes and changes of some cardiovascular/ cerebrovascular prognostic factors after carotid stenting, 40 patients with symptomatic carotid stenosis 70% or greater, who met the set criteria for carotid stenting, were recruited for this study. Baseline blood flow velocity (BFV) and pulsatility index (PI) of the middle cerebral artery and the small orbital vessels were obtained using transcranial Doppler (TCD) and/or color duplex scan. The baseline prognostic factors, such as CO<sub>2</sub> reactivity, heart rate variability (HRV) and baroreflex sensitivity were assessed with previously described non-invasive methods. These hemodynamic variables and the prognostic factors were followed up regularly after stenting at one week, two week, one month, three and six months. We found that the BFV and PI in the ipsilateral middle cerebral artery and the central retinal artery were increased significantly at one week. All the reversed ophthalmic flow became forward in direction at one week. All the prognostic factors were improved in the majority of patients after stenting. We concluded that carotid stenting improves the cerebral hemodynamics and alters cardiovascular/cerebrovascular prognostic factors.

## Angiography Findings in Super-early Period of Ischemic Stroke

SVIII

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**Objectives**

To evaluate the frequency and localization of the involved arteries in ischemic stroke with 6 hours after onset.

**Data and Methods**

The patients suffered from ischemic stroke with 5-30 points of NIHSS and confirmed by brain CT. All subjects underwent high selective angiographies for the observation of aorta, carotid arteries, vertebral arteries, and all the intracranial arteries. The degree of stenosis, the localization and the numbers of the arteries involved and the morphology of plaque or the stenosis were assessed.

**Results**

Thirty patients were enrolled with 23 male and mean age of 56.7 years. The angiographies were performed with average time of 218±64 minutes after the onset of stroke. The brain CT found old lesions in 2 cases and suspected hypodense lesions in 9. Angiography showed occlusive finding of cerebral arteries in 86% of the patients, among them 77% located in anterior circulation and 23% posterior. Another 10 asymptomatic arteries were found. Angiograms were normal in 13%. The internal arteries and middle cerebral arteries is most frequently involved in this series. Vertebral arteries were the most common involved one in posterior circulation. Only were the residual ending of occlusive arteries or high grade of stenosis shown in high selective angiogram. The patients with the symptoms of posterior circulation were angiographed about 30 minutes later than the anterior (246.6±87.1, 218.9±65.2 minutes, respectively).

**Conclusion**

Most of patients with ischemic stroke with 6 hours were documented with definitive occlusion of cerebral arteries. The options of treatment should base on the location, the number and the morphology of involved arteries.

## The Dynamic Study of Stroke MRI in Hyperacute Stroke Patients with Thrombolysis

SVIII

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**Objectives**

Identification the penumbra of patients with acute ischemic stroke was very importance for the treatment and prognosis in clinical. In acute ischemic stroke, volume mismatch between diffusion- and perfusion-weighted MRI (DWI, PWI) map can be seen and this mismatch may be correlated with the ischemic penumbra. We studied the diagnostic and prognostic value of stroke MRI for the initial evaluation and follow-up monitoring of patients with hyperacute ischemic stroke.

**Methods**

Stroke MRI [DWI, PWI, MRAngiography(MRA), T2-weighted imaging(T2-WI)] was performed in 19 patients within 6 hours after symptom onset, and on days 1,2 and 7. 19 patients were divided 10 having thrombolysis (thrombolysis group) and 9 having LMWH (Low Molecular Weighted Heparin, 4100IU, subcutaneously, twice a day) as control group. We assessed clinical scores (NIHSS, CSS, ADL) at days 1,2 and 7. Furthermore, we performed volumetric analysis of infarct volumes on days 1,2, and 7 as shown in DWI, PWI, and T2-WI.

**Results**

There were no difference in the age, the time of treatment, the scale of anamnesis, concomitant, and initial NIHSS, CSS between the thrombolysis and control groups ( $p>0.05$ ). 4/10 patients recovered in thrombolysis group, but none recovered in control group ( $p<0.05$ ). In thrombolysis group, 7 patients were performed MRA and 8 patients were performed PWI/DWI. We found the mismatch (PWI>DWI) sign in 4 recovered patients and 3 had no vessel occlusion, 1 recanalized after 24 hours, but the other 4 patients with PWI ≤ DWI mismatch sign were deprivation (one patient death) and 3 patients had MCA occlusion.

In control group, we performed the dynamic stroke MRI in a 52 years old patient. The mismatch sign of PWI>DWI was found beyond 6 hours, MCA occlusion was showed at same time, and MCA recanalized after 24 hours and 72 hours. After 7 days, the volume of DWI was same the T2-WI and PWI=DWI, this patient had worse outcome.

**Conclusions**

There were 50 percent patients with the mismatch sign of PWI>DWI in hyperacute ischemic stroke. This sign indicated that the tissue in the penumbra may be salvageable, the outcome of patients with thrombolysis was better. If there were no sign of PWI>DWI mismatch, and MCA occlusion, then the thrombolysis was not safe. The efficiency of thrombolysis was correlated the sign of PWI>DWI mismatch in patients with hyperacute stroke.

## SYMPOSIUM IX - MOVEMENT DISORDER

## Efficacy, Safety and Tolerability of Pramipexole Among Chinese Patients with Parkinson's Disease

SIX

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**Objectives**

We studied the efficacy, safety and tolerability of pramipexole among Chinese patients with PD.



## Methods

This was a multicenter (2 sites in HK, 3 sites in Taiwan), randomized, double-blind, flexible-dose, placebo-controlled, parallel-group study. This study consists of a 7 week dose-escalation period, followed by an 8 week maintenance period. The primary efficacy variable was the change from baseline to the end of treatment for the UPDRS parts II and III combined scores.

## Results

A total of 150 Chinese patients with PD were randomized to receive either pramipexole (n=77) or placebo (n=73). Forty-three randomized patients were not on levodopa. The mean improvement in the UPDRS parts II and III combined scores at the end of 15 weeks was significantly greater in the pramipexole group than in the placebo group (minus 12.14 points vs. minus 2.45 points;  $p < 0.0001$ ).

Pramipexole was effective regardless of whether or not patients were on concomitant levodopa therapy. Adverse events were slightly more common in the pramipexole group (63/73; 86.3%) than in the placebo group (55/77; 71.4%). Common adverse events seen in the pramipexole group were dizziness (27.4%), constipation (20.6%), nausea (15.1%), dry mouth (12.3%), dyskinesia (12.3%), hallucinations (12.3%) and somnolence (12.3%). Most of these adverse events were of mild severity. Thirteen patients (7 pramipexole, 6 placebo) discontinued due to adverse events.

## Conclusions

Pramipexole was significantly more effective in improving UPDRS scores than placebo among Chinese patients with PD. It was safe and was well tolerated. Its most common adverse events were typical of dopamine agonists.

## Genome-wide Scanning for New Types of Spinocerebellar Ataxia

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Autosomal dominant spinocerebellar ataxia (SCA) is a clinically heterogeneous group of disorders. The genes for SCA1, SCA2, SCA3, SCA6, SCA7, SCA8, SCA10, SCA12, SCA16 and SCA17 have been identified. Expansions of a CAG, CTG or ATTCT repeat sequence within these genes may result in clinical manifestations. Five additional loci for SCA4, SCA5, SCA11, SCA13, and SCA14 have also been mapped to chromosomes 15q14-21.3, 11p11-q11, 16q22.1, 19q13.3-13.4 and 19q13.4-qter, respectively.

We have identified and clinically characterized three pedigrees with un-assigned autosomal dominant SCA. All of the affected individuals had cerebellar ataxia on repeated neurological examinations, as well as slight to moderate atrophy of the cerebellum in neuroimaging studies. The age of onset was variable, with the range being 10 to 55 years, and the mean  $\pm$  SD being  $23.3 \pm 11.7$ ,  $25.3 \pm 11.7$  and  $33.5 \pm 6.8$  years, respectively.

Anticipation in disease onset was noted in all of the families, suggesting that the expansion of unstable tandem repeats is a likely mechanism of mutation in the responsible genes of these families, as seen in other SCAs with similar mutations. Aside from slowly progressive gait ataxia, other neurological signs included gaze-evoked nystagmus, ocular overshooting and saccadic pursuit, hyperreflexia/hyporeflexia, and limb hypotonia. None of them showed abnormalities in the autonomic nervous system, sensory perception, or cognitive functions. No patients had epilepsy, myoclonus, parkinsonism, or sensory neuropathy. Previously

known SCA types had been excluded by direct detection of triplet repeat expansion of the ten known SCA genes, as well as by linkage analysis at the additional five loci. Whole genome mapping has successfully uncovered at least one new locus for SCA.

## Clinical and Molecular Advances in Autosomal Dominant Cerebellar Ataxias

SIX

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Autosomal-dominant cerebellar ataxias (ADCA) may present as progressive or paroxysmal disorders, while the progressive ataxias have been named spinocerebellar ataxias (SCA), the paroxysmal disorders are designated episodic ataxias (EA). Until now twelve genetic types of autosomal-dominant hereditary ataxia have been recently identified and the genes responsible for most of them have been cloned. Molecular identification of the ataxias is important to determine the disease prevalence and its history in various populations.

Several genetic distinct types of autosomal-dominant ataxia have been mapped: SCA<sub>1</sub> to chromosome 6p, SCA<sub>2</sub> to 12q, SCA<sub>3</sub>/MJD to 14q, SCA<sub>4</sub> to 16q, SCA<sub>5</sub> to 11cen, SCA<sub>6</sub> to 19q, SCA<sub>7</sub> to 3p, SCA<sub>8</sub> to 10q24, SCA<sub>10</sub> to 22q13, SCA<sub>11</sub> to 15q14-21.3 and SCA<sub>12</sub> to 5q31-33.

To perform clinical type and molecular analysis of 86 Chinese families affected with SCAs (SCA<sub>1</sub> 5, SCA<sub>2</sub> 9, SCA<sub>3</sub>/MJD 62, SCA<sub>4</sub> 4, SCA<sub>7</sub> 2, SCA<sub>12</sub> 4), the disease-causing gene of SCA1,2,3,7 have been cloned and the mutation identified as an expansion of CAG trinucleotide repeat in gene coding region. SCA<sub>4</sub> and SCA<sub>12</sub> diagnosed by typical clinical features and electromyography. At the same time the anticipation relation to the instability of trinucleotide repeat was identified.

1. We reported and performed clinical, pathological investigation systematically of Chinese SCA<sub>3</sub>/MJD for the first time and found the biggest pedigree of Asia. (published in Bethesda Md. 1991)
2. We analysed the size of (CAG)<sub>n</sub> array in China for the first time and found that it is 14-40 in normal chromosomes, whereas it's 72-86 in affected chromosomes; the inter-generational changes of CAG trinucleotide repeats are unstable and it was considered that it is molecular basis of the clinical phenomenon of anticipation. As higher as the number of repeat goes up, the age of onset is becoming earlier. We reported the highest number (86) of CAG repeat and the earliest age of onset. (published in Neurology vol. 48 1997)
3. In order to narrow the candidate region of this gene, we made a linkage study of Chinese MJD pedigrees with 13 microsatellite markers on 14q and then located it in 3cM region between D14S280 and D14S81 which is the precise region internationally. (published in Hum Mol Genet. vol.5 1996)
4. It is the first time that we found that the CAG repeat expansion was associated with 3' CGG/GGG polymorphism and implied that it was one of the causes of (CAG)<sub>n</sub> expansion instability. There was no same report in the world.
5. This investigation has established an analysis system of repeat sequence and it can be used in analysis of CAG repeat and clinical examination, not only in MJD but also in other inherited neurodegenerative disorder, for example, SCA<sub>1</sub>, SCA<sub>2</sub>, DRPLA, etc. Recently we reported SCA<sub>2</sub> in China for the first time which has been published in Neurology vol.51 1998 and SCA<sub>7</sub> in Archives of Neurology vol.57 Oct 2000 and SCA<sub>1</sub> in Archives of Neurology vol.58 May 2001.

## Writing for a Neurological Journal: Tips from the Other Side of the Editor's Desk on How to Get Your Paper Published

SX

**Richard Hughes**

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Years of writing papers and editing two neurological journals and now the Cochrane Neuromuscular Disease Review group systematic reviews in the Cochrane Library give the author a special perspective on writing for neurological journals. He will try to pass on some useful tips, which will enhance your chances of having your paper accepted in the journal of your choice. The lecture will cover the following topics:

1. Subject matter: is your material ready for publication?
2. Choice of journal: is the journal good enough for your work? Is it the right journal? What is its citation index?
3. Article format: have you read and carefully obeyed all the instructions for section headings and submitting your article?
4. Check List:
  - a. Title: is this short and informative?
  - b. Authors: have they all contributed and how and has anyone been left out?
  - c. Introduction: give the background to help the novice understand and explain the object of the study. Do not give the results.
  - d. Methods: explain the methods including the statistics so that others could replicate your work.
  - e. Results: let your results flow in a logical sequence. Use tables and figures when appropriate but do not give the data twice.
  - f. Discussion: this should be relevant and not repetitive, stating how your results advance knowledge and point to future research.
  - g. Acknowledgements: don't forget.
  - h. References: use the journal's format and reference managing software.
5. Style of writing: unfortunately many scientists are poor writers. This applies to native English speakers as much or more than others. Consider purchasing a book on English writing style. Some common errors will be illustrated.
6. Confidentiality: respect the confidentiality of your patients and obtain written permission to publish even anonymised case reports.
7. Randomised controlled trials: special rules (CONSORT guidelines) govern reporting randomized controlled trials.
8. Scientific fraud: the authors must be able to guarantee all the results and retain the records on which they are based for a minimum of seven years, longer in the case of clinical trials.
9. Checking: use spell check software and have all the authors double check the final version of your manuscript before submission.
10. Rejections and resubmission: if your paper is rejected and the grounds seem to you incorrect consider appealing. Only do this if you have strong grounds. It is usually better to start again with a different journal.

Good luck.

## Evidence-based Neurology: Thoughts and Practice

SX

**Ming Liu**

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Evidence-based medicine (EBM) is the integration of best research evidence with clinical expertise and patient values. EBM is becoming

widely accepted by neurologists. To improve neurological patient care we need evidence-based neurology and good evidence is essential for practicing evidence-based neurology.

The order of strength of evidence for therapies (from strongest to weakest) is: (1) systematic review of good quality randomised controlled trials (RCTs) (strongest); (2) one good quality RCT; (3) well-designed controlled trials without randomisation; (4) other good non-experimental studies; (5) opinions of experts based on clinical experiences (weakest). It is important for a clinical practitioner to know how to find the current best evidence and for a clinical researcher to know how to produce good quality research evidence.

Good evidence can be found from paper journals (ACP Journal Club, Evidence-Based Medicine, Clinical Evidence) and electronic databases (Best Evidence, Cochrane Library etc). Cochrane Library ([www.cochranelibrary.com](http://www.cochranelibrary.com)) is the best source for evidence of effects on health care interventions including neurology area. Evidence-based guidelines on neurological disorders are also useful for busy first line clinicians.

For providing and producing evidence, we have set up a database of neurological clinical researches published in Chinese. We also conducted several systematic reviews on stroke and other neurological disorders. Some have been published in the Cochrane Library and Paper journals. Through these work we found that the number of high quality evidence is far from the needs for neurological clinical practice. Particularly for therapies, truly randomised controlled trials are too few to use easily in neurological clinical practice compared with in cardiology and oncology areas. Using of unproven therapies is quite common. Therefore, we thought that currently the more urgent thing for practicing evidence-based neurology is to have more good evidence available for clinical practice. As a result of our systematical review on acupuncture for acute stroke, we initiated a multi-centre randomised controlled trial to answer the question of effectiveness of acupuncture for acute ischemic stroke. The pilot study is underway.

Various barriers exist for conducting more high quality RCTs in China, such as lack of knowledge on EBM, lack of awareness of methodology importance on clinical studies. Lack of understanding of ethic issues on RCTs, lack of expertise on methodology of conducting high quality RCTs and lack of resources. However, things are changing gradually along with the disseminating of knowledge on clinical epidemiology and EBM. More and more clinicians are willing to collaborate in multi-center trials and in future, more good evidence for neurological care will be produced in China.

## Applying Basic Science to Clinical Neurology

SX

**Meng-cheong Wong**

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Neurologic diagnosis and treatment have much to gain from recent advances in basic science. Much is becoming rapidly possible.

Hereditary neurologic disease diagnosis has been refined by neurogenetic testing. Presymptomatic diagnosis is becoming increasingly common, with implications for neuroprotective therapies.

Brain tumour therapy is currently unsatisfactory, particularly for malignant gliomas, which constitute the most common primary brain tumour. Gene therapy is currently in clinical trials. Technical refinements continue to undergo testing in research models.

Cell therapy for degenerative neurologic diseases is intriguing and this evolving field spans progenitor and stem cell paradigms.

Stroke is a leading cause of morbidity and mortality. However our understanding of vascular pathology in stroke patients is fragmentary. Cellular and molecular events need to be elucidated.

Illustrative examples from our group's experience will be discussed, including microvascular ultrastructure, endothelial gene expression, gene and cell therapies in attempts towards improving the diagnosis and treatment of neurologic diseases.

## The Association of Insulin and the Plasma Concentration of $\beta$ -amyloid in Alzheimer's Disease

SS I

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### Objectives

To study the association of insulin and the plasma concentration of  $\beta$ -amyloid in Alzheimer's disease.

### Methods

All cases were the participants who diagnosed in the investigation in Shanghai between 1997 and 1998. The concentration of plasma insulin and  $\beta$ -amyloid were tested Radiological Immunology Analysis.

### Results

Patients with AD had higher insulin level ( $25.56 \pm 19.12$ ,  $\mu\text{IU/ml}$ ) than normal control group ( $15.88 \pm 11.05$ ,  $\mu\text{IU/ml}$ ). There was significantly different between the two group ( $H=10.5$ ,  $p<0.05^\circ$ ). Compared with control group, patients with AD had higher  $\beta$ -amyloid level ( $21.24 \pm 9.4$  pg/mL) than normal control group ( $16.03 \pm 7.25$  pg/mL). There was significantly different between the two groups ( $H=13.1$ ,  $p<0.05$ ). With aging, the  $\beta$ -amyloid concentration of two groups didn't change much before 90 years old, the insulin concentration decreased with no significance. By multiple regression the  $\beta$ -amyloid level had positive association with insulin ( $r=0.088$ ,  $p>0.05$ ), GDS (Global Deterioration Scale) ( $r=-2.528$ ,  $p<0.05$ ), aging ( $r=0.048$ ,  $p>0.05$ ) and negative association with course of disease.

### Conclusions

There was association between insulin and  $\beta$ -amyloid concentration in Alzheimer's disease.

### Key words

Alzheimer's disease; insulin;  $\beta$ -amyloid; plasma

## Demographics and Clinical Characteristics of Myasthenia Gravis in Singapore

SS I

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### Objectives

To describe the demographic and clinical features of myasthenia gravis (MG) encountered at a single institution in Singapore.

### Methods

A retrospective analysis of 133 cases of MG studied at a major neurologic referral centre in Singapore over a 7-year period from January 1994 to December 2000.

### Results

A total of 133 cases were reviewed from January 1994 to December 2000. Ninety-two cases were diagnosed after 1993. The mean age at onset was 44.2 years. There was a slight female predominance with a female to male ratio of 1.56 : 1. The distribution of patients with MG included 90.4% Chinese, 5.6% Malays, 4.0% Indians, and none from the other ethnic groups. After adjustment for the racial composition in Singapore, the likelihood of MG occurring in the ethnic Chinese was three times that of the other races (Chinese : Indian : Malay – 2.93 : 1.26 : 1). At the onset of symptoms, 55.8% had ocular MG and 44.2% had generalised MG.

The mean duration of disease was 77.7 months (median 39.8 months), with an average follow-up period of 51.0 months (median 28.5 months). During the follow up period 36.1% continued to have localized disease, with two patients having bulbar symptoms only. Of the 26 ocular MG with secondary generalization, half of them generalized within 26.4 months. Thymoma was present in 18.8% of patients (27.1% of generalised MG, 4.2% of localized MG,  $p=0.001$ ), and accounted for almost half of those patients who underwent thymectomy. 29 patients had a total of 34 associated autoimmune conditions. All were Chinese with a female to male ratio of 4.8 : 1.

Autoimmune thyroid disease topped the list with 19 patients, followed by systemic lupus erythematosus with six patients. Overall, 65.2% of patients had disease under control either by pyridostigmine, immuno-suppressants, or combination of the two. Ocular MG did better with 16.7% in complete remission without any medication, compared to 4.8% of generalised MG ( $p=0.009$ ).

### Conclusions

The prevalence of MG at a single institution in Singapore was three times more common in ethnic Chinese than the other ethnic groups. Ocular MG constituted a significant proportion of MG and was higher than series reported outside Asia. While the prevalence of thymoma was high, the prevalence of associated autoimmune conditions was comparable to other studies.

## Hyperhomocystinaemia in Ischaemic Strokes from a Multi-racial Population in Malaysia

SS I

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### Objectives

Hyperhomocysteinemia has been established to have a strong and graded association with ischaemic strokes. There has been no previous studies into homocysteine levels of Malaysian patients with ischaemic strokes in contrast to published studies in Western populations. Accordingly, this pilot study had the following objectives (1) to determine the prevalence and degree of hyperhomocysteinemia among local patients admitted with confirmed ischaemic strokes (2) to ascertain if there were any significant differences in homocysteine levels between the various ethnic groups and between lacunar and large vessel strokes.

### Methods

This case-control study was based on consecutive first ever ischaemic stroke patients admitted to University of Malaya Medical Centre (UMMC) from June to November 2000. Demographic and clinical information including known stroke risk factors were collected. Patients with known factors that affected homocysteine levels were excluded. Non fasting blood samples were collected within 1 week (day 3-4) of admission and processed in a standardized manner. Analysis was performed using a commercially available immunoassay. Subjects with comparable age and gender with no prior history of strokes or other known vascular diseases were recruited as controls. Patients above the 75<sup>th</sup> percentile of the control group was labelled as hyperhomo-cysteinemic while those in the 95<sup>th</sup> percentile group was labelled as moderately hyperhomocysteinemic.

### Results

83 stroke patients were assessed which consisted of 52 males and 31 females. There were 80 subjects in the control group. The prevalence of mild hyperhomocysteinemia was 30% (values

from 12.0 micromol/l to 14.99 micromol/l) while moderate hyperhomocysteinemia was 23% (values above 15 micromol/l). The mean plasma homocysteine level for stroke patients was 13.4 micromol/l (95% CI 11.82-17.6 micromol/l), significantly higher than in controls at 10.5 micromol/l (95% CI 9.9-11.1 micromol/l) ( $p < 0.0001$ ). No significant differences were found in between various ethnic groups and between lacunar and large vessel strokes. Multivariate statistical methods showed homocysteine to be an independent risk factor, adjusted for the usual stroke risk factors. Odds ratio of those with moderate hyperhomocysteinemia and stroke was 6.5 (95% CI 2.2-20.6) ( $p < 0.001$ ) compared with control subjects. In mild hyperhomocysteinemia, the odds ratio for ischaemic stroke was 3.2 (95% CI 1.6-6.5) ( $p < 0.001$ ).

### Conclusions

Hyperhomocysteinemia is found in 53% of ischaemic stroke patients within UMMC. Homocysteine appears to be an independent ischaemic stroke risk factor in which there is a graded association. This is greater in those with moderate to severe hyperhomocysteinemia. Dietary and genetic factors may play a role.

## Miller-Fisher Syndrome: Experience from a Regional Hospital

SS I

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### Background

Miller-Fisher syndrome (MFS), characterized by ophthalmoplegia, ataxia, and hypo- or areflexia, is considered a rare clinical variant of Guillain Barré syndrome (GBS). There is not much data on the electrodiagnostic (EDx) findings in MFS. Previous series reported predominant sensory nerve conduction abnormalities with minimal motor involvement.

### Method

Admission records to the Neurology ward and EDx reports of the Neurodiagnostic Unit from Jan 1998 to June 2001 (42 months) were reviewed to identify cases of MFS. Their clinical features, investigation findings, and treatment outcomes are described.

### Results

Out of the 26 cases of GBS, 5 patients (19%) fulfilled the clinical criteria for MFS. Mean age of patients was 45 (range 30-58) and M:F ratio was 2:3. All patients had an antecedent flu-like illness. The symptoms evolved over 4 to 10 days. Clinical manifestations, besides ophthalmoplegia (complete in 2), cerebellar signs, and hypo- or areflexia, included sensory disturbance (3/5), generalized weakness (2/5), bilateral upgoing planter responses (1/5), pain (2/5), iridoplegia to light (1/5), ptosis (2/5), unilateral facial palsy (1/5), vertigo (1/5), and bulbar dysfunctions (3/5). Cerebrospinal fluid protein level was elevated in only one case (20%), as compared with 71% of the non-MFS GBS cases. GQ<sub>1b</sub> autoantibody titre was significantly raised in 4 cases (80%, mean 84.5 EIA U, range 43 to >160). EDx abnormalities included mild attenuation of sensory and compound muscle action potential amplitudes, prolongation of distal motor latencies, reduced F-persistence, and/or neurogenic EMG changes. Such mild changes were present in all cases but none fulfilled the EDx criteria for demyelination. Follow-up studies showed recovery of most of these abnormalities. MRI was performed in 4 cases. A small non-enhancing midbrain lesion, suspicious of focal demyelination, was found in one patient. Two cases were treated with plasmapheresis (PE) and 2 received intravenous immunoglobulin (ivIg). Another patient was given ivIg after developing shock during PE. None of the patients needed ICU admission or died, as compared with 29% and 9.5%, respectively, of the non-MFS GBS cases. The mean length of hospitalization was 17 days (range 9-23). On follow-up assessment, all patients had complete clinical recovery.

### Conclusions

From our observation, MFS is not that uncommon with an incidence of 0.3 case per 10,000 population/year. Many of our MFS patients had clinical features overlapping with GBS, but their clinical courses were relatively benign. EDx abnormalities, although more extensive than previously described, were rather subtle.

We treated our patients with PE or ivIg and the clinical and electrodiagnostic outcomes were satisfactory. However, because of our small patient population and lack of a control group, we cannot conclude whether PE or ivIg is definitely beneficial in MFS.

## Seasonal Variation in the Occurrence of Stroke in Taiwan

SS I

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### Background and Purpose

Seasonal influence on the occurrence of stroke has been reported for half a century. However, seasonal variation in different types of stroke was seldom reported in Taiwan. The present study aimed to assess the seasonal variation in the occurrence of different types of stroke.

### Methods

During 1995-1999, there were 4,014 patients (2,327 males and 1,687 females; mean age, 62.8 years; age range, 1-100 years) with first-ever acute stroke registered at the National Taiwan University Hospital. Stroke was categorized as cerebral infarct (CI), cerebral hemorrhage (CH), subarachnoid hemorrhage (SAH) and transient ischemic attack (TIA). CI and CH were further classified into several subtypes. An Edwards test was used to analyze the seasonal variation of stroke and its subtypes.

### Results

Of stroke types, 2657 had CI; 933, CH; 240, SAH; and 183, TIA. Seasonal variation was significant for CH in men, and CH patients aged  $\geq 45$  years. Seasonal variation was significant for overall stroke, CI and CH ( $p = 0.0005$ , 0.05 and 0.0002), but not for SAH and TIA ( $p = 0.1$  and 0.7). The peak occurrence of CI and CH was in May and March separately, not in winter. For CI subtypes, seasonal variation was significant in cardioembolism and stroke of undetermined etiology, but insignificant in large artery atherosclerosis, lacune and other specific etiologies of stroke. For CH subtypes, only hypertensive type had strong seasonal variation.

### Conclusions

The seasonal variation differs significantly among different types of stroke, CI and CH. The peak occurrence of stroke is not in the coldest season and this remains to be determined.

## SCIENTIFIC SESSION II

### First Results of Autologous Haematopoietic Stem Cell Transplantation for Progressive Multiple Sclerosis in China

SS II

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### Objectives

To evaluate the clinical effect and toxicity of treating progressive multiple sclerosis (PMS) with autologous haematopoietic stem cell transplantation (HSCT).

## Methods

3 patients with PMS were treated with HSCT. Patients were severely disabled, with EDSS scores of 6.5- 8.5. Cyclophosphamide and G-CSF were used for stem cell mobilization. Antithymocyte globulin (ATG) was given for in vivo T cell-depletion in one patient and CliniMACS was used for T cell-depletion in another two patients. The autologous haematopoietic stem cells were reinfused after conditioned by Cyclophosphamide/TBI or BEAM regimen. G-CSF was used to help haematopoietic and immunologic reconstitution.

## Results

Though some mild, transient neurotoxicity were observed in these three patients after stem cell infusion, all these three patients obtained clinical remission after HSCT. In the first patient, the gadolinium-enhanced lesions on MRI in T1-T4 levels disappeared and the examination results of the neuroelectrophysiology and T cell subgroup were improved obviously at 3 months after HSCT. The EDSS was considerably improved from 8.0 to 3.0 at 12 months after HSCT.

In the second patient, the disability remained stable (EDSS of 8.5) during the follow-up of 3 months after HSCT. In the third patient, the disability was improved on EDSS from 6.5 to 6.0 to date, only 1 month after HSCT. There was no relapse during the follow up of 1-12 months in these three patients.

## Conclusions

Autologous HSCT is effective and safe for PMS. However, these observations need confirmation and long-term follow-up is necessary.

## Single Fiber Electromyography in 78 Patients with Amyotrophic Lateral Sclerosis SS II

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## Objective

To investigate the changes and pathophysiological mechanism and clinical values of single fiber electromyography (SFEMG) in 78 patients with amyotrophy lateral sclerosis (ALS).

## Methods

Routine EMG, nerve conduction velocity and extensor digitorum communis SFEMG were measured in 78 patients (male 51, female 26) who were diagnosed by history, clinical features and neurophysiological tests compared with normal controls.

## Results

Normal sensory nerve conduction was found in all subjects. Routine EMG showed neurogenic lesions in muscles innervated by two spinal regions at least. SFENG showed that remarkable increased jitter, block and fiber density (FD). Jitter ranged from 30-178 $\mu$ s (mean 80.2 $\mu$ s); the value of jitter>55 $\mu$ s ranged from 5%-100% (mean 60.5%). The ratio of block ranged from 0-90% (mean 28.1%). FD ranged from 1.4-4.1 (mean 2.61). There were remarkable increased jitter, block and FD in 51 patients with definite or probable ALS.

It was also found that there was a negative correlation between extensor digitorum communis strength grades and increased jitter with or without block and FD ( $P<0.01$ ).

## Conclusion

1. SFEMG was the most sensitive in the diagnosis of definite or probable ALS.
2. There was a negative correlation between the increased jitter and block and FD and degrees of muscle weakness.
3. Increased jitter and block and FD probably indicated continuous denervation and reinnervation with litter time for forming mature sprouts and motor end plates.

## Critical Closing Pressure can be Used to Estimate the Lower Limit of Cerebral Blood Flow Autoregulation SS II

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## Objectives

Cerebral blood flow autoregulation (CBFA) plays an important role in occurrence and development of cerebrovascular diseases. However, so far there has not been an ideal method to determine the function and the range of the individual subject CBFA without blood pressure change. The aim of the present study was to establish a new method to assess the lower limit of CBFA by cerebrovascular critical closing pressure.

## Methods

The blood flow velocity of middle cerebral artery was monitored by transcranial Doppler sonography, and the femoral blood pressure was recorded simultaneously by physiological multimeter on male normotensive Sprague-Dawley rats (NR) and renovascular hypertensive rats (RHR). After cerebrovascular critical closing pressure (CCP) was derived from the zero flow pressure as extrapolated by regression analysis of instantaneous arterial pressure/middle cerebral artery flow velocity relationships, the lower limit of CBFA was figured out by CCP.

At the same time the lower limit on the same rat was evaluated by hemorrhage hypotension again as controls. Brain sections and middle cerebral artery, basilar artery and carotid common artery sections stained with hematoxylin-eosin and Weigert resorcin acid-azaleine were examined under a microscope and were analyzed by an image auto-analysis system to determine morphological changes of cerebral vessels.

## Results

At 17th week after renal artery constriction in RHR, the lower limits of CBFA estimated by CCP in NR and RHR were 70.88 $\pm$ 24.05 mmHg and 107.73 $\pm$ 38.82 mmHg respectively, which were both significantly identical to the results observed by traditional hemorrhage hypotension as control (69.74 $\pm$ 23.07 mmHg and 109.92 $\pm$ 41.00 mmHg). And the lower limits of CBFA by CCP were highly correlated to the media thickness of cerebral arteriole, but only to arteriole in whole cerebrovascular system, both in NR and RHR. At the same time the lower limit in RHR was moving up with the blood pressure increasing.

## Conclusions

The way deriving the lower limit of CBFA from the CCP is an ideal method to determine the range of the individual animal's CBFA without blood pressure change.

## Randomised Controlled Trial in Treatment of Carpal Tunnel Syndrome SS II

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## Objective

Despite the widespread use of corticosteroid injection as a mode of treatment in carpal tunnel syndrome (CTS), there are few randomized controlled trials in confirming its usefulness. There have been reports that oral steroids are beneficial; the rationale is that reducing congestion within the carpal tunnel would relieve nerve compression. We compared the effectiveness of low-dose, short-term oral prednisolone against local methylprednisolone injection in the treatment of CTS in a prospective randomized, double blind, placebo-controlled study of patients.

## Method

We recruited patients with sensory symptoms suggestive of CTS and confirmatory electro-physiological results. Patients were randomly assigned to one of two groups: the first group received oral placebo daily for 10 days and a single 15mg methylprednisolone acetate injection locally into the carpal tunnel and the second group received prednisolone 25mg daily for 10 days and the same volume of saline injection. The primary endpoint variable was the Global Symptom Score (GSS). The GSS ranges from 0 (no symptoms) to 50 (most severe symptoms) and was recorded at baseline, two, eight and twelve weeks. Two samples t-test was used for comparison between the oral steroid group and the injection group during each time phase.

## Results

30 patients were randomized to the steroid injection and oral group and 30 patients to the oral prednisolone and placebo injection group. The demographic and clinical characteristics were comparable. Mean GSS at baseline was 25.0 (SD 6.4) for the injection group 25.7 (SD 8.3) for the oral group,  $p=0.70$ . Significant improvement for the injection group was present at 8 weeks ( $p=0.002$ ) with mean GSS of 13.7 (SD 8.3) for the injection group and 20.8 (SD 8.7) for the group; and at 12 weeks ( $p=0.004$ ) with mean of 14.3 (SD 8.4) for the injection group and 21.4 (SD 9.6) for the oral group. Side effects were minimal in both groups and there were no dropouts.

## Conclusion

Our study shows that local steroid injection was superior to oral corticosteroids in patients with CTS over a three months period. Patients in the oral prednisolone group had improved scores for only up to 8 weeks.

## Causes of Aspirin Failure in Ischaemic Stroke

SS II

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2. Private Neurologist.

## Objectives

To investigate the causes and factors associated with of drug treatment failure in patients who developed ischaemic stroke while already on aspirin.

## Method

We screened patients presented with acute ischaemic stroke from 1 Jan to 31 March 2001 prospectively, and reviewed case files of acute stroke patient from Nov to Dec 2000 retrospectively. We identified patients who were already on aspirin continuously for at least 3 months for any reason before the onset of stroke. Patients' demographic data, BMI, stroke risk factors, drug compliance, nature of recurrent stroke were recorded. We based on American Heart Association Scientific Statement to determine whether patients' modifiable stroke risk factors were satisfactorily controlled or not.

## Results

There were 42 case identified. Mean NIHSS was 4.7.

Nine patients were in atrial fibrillation (21.4%). Sixteen had DM (38.1%), 31 had HT (73.8%), 20 had IHD (47.6%), 25 had previous history of CVA or TIA (59.5%). Twenty-one had hyperlipidaemia (50%), mean TC was 5.09 mmol/l. Eleven were considered to be overweighted (26.2%), with mean BMI of 23.4. Only one-quarter of DM patients had HbA1c < 7% and about half of HT patients had optimal BP control. There was no active smoker. 71.4% claimed to have good drug compliance. Two patients had significant carotid stenosis suggested by carotid duplex ultrasound.

Only 4 patients (16.7%) in whom all risk factors were optimally controlled and no other underlying cause was identified.

## Conclusions

Many of the stroke risk factors were not optimally managed (DM, HT, AF, lipid) in patients with "aspirin failure". These factors should be critically reviewed in patients with recurrent ischaemic stroke, before concluding aspirin treatment is ineffective.

## POSTER PRESENTATIONS

### MRA Features of Diabetes Mellitus During Acute Cerebrovascular Disease

P 1

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## Objectives

To investigate the relations of acute cerebral vascular disease for diabetic mellitus patients and MRA, it was analyzed 43 cases of diabetes.

## Methods

All the patients were examined by T<sub>1</sub>W and T<sub>2</sub>W imaging and MRA with 3D-TOF.

## Results

There are 27 patients with MRA abnormal in 43 cases, mainly changes:

1. Single or multiple breaches stenosis of carotid artery.
2. Main breaches obstruction.
3. The vessels decrease in the some areas.
4. The occurs of the re-circulation breaches.
5. The vessels "stiffness" change from artherosclerosis.
6. The section stenosis and expanding.
7. The abnormal rate of MRA was not relations with the clinical degree of patients, but it was the values with the suffered duration.

## Conclusions

It was suggested that the degrees of cerebrovascular lesions would be evaluated by the examination with MRA for diabetes mellitus, and there are the important roles in prevent and management for diabetic patients with stroke.

### Ankle-brachial-pressure Index in Ischaemic Stroke

P 2

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## Objective

To investigate the effect of the ankle-brachial-pressure index (ABPI) - the ratio of the ankle to the brachial systolic blood pressure - on indication of occlusive atherosclerotic disease in the brain.

## Methods

Study population consisted of 100 patients with ischaemic stroke (group-1) and 100 control whose paired each of the patient with age- and gender-matched (group-2). Systolic blood pressure was measured three times in the left arm and at the left ankle with an automated recorder, while the subject was lying down. The cuff was removed and replaced between measurements. The mean of these measurements was used to calculate the ABPI.

## Results

The mean  $\pm$  SD age of group-1 (65 men, 35 women) was 63.6 $\pm$ 12.5 years (range 31~90 years), and the mean  $\pm$  SD age of group-2 (65 men, 35 women) was 64.1 $\pm$ 13.2 years (range 34~85 years). There was not significant difference between the ages of two groups. However, the mean  $\pm$  SD ABPI of group-1 was 0.92 $\pm$ 0.07, and the mean  $\pm$  SD ABPI of group-2 was 1.10 $\pm$ 0.06.

There was a significant difference between the ABPI of two groups ( $p < 0.01$ ). In addition, ABPI less than 0.90 is 51% in group-1, and 4% in group-2. There was also a significant difference between the two groups by  $\chi^2$  test ( $p < 0.01$ ).

### Conclusions

Ischaemic stroke is typically characterized by occlusion of one or more cerebral arteries secondary to atherosclerosis. Since carotid stenosis and a low ABPI can both be regarded as markers of generalised arteriosclerotic disease, one might have expected a similar prognosis in the ischaemic stroke.

Ogren et al suggested that an ABPI less than 0.90 is a more powerful marker of generalised arteriosclerotic disease than is an ultrasonographically detected carotid stenosis of 30% or more. Our results showed that ABPI is much less in ischaemic stroke than in control, and indicated that a low ABPI can be regarded as a useful marker of ischaemic stroke. Since ABPI measurement is very easy to manipulating, it can be clinically used to monitor progression of severity of obstruction in cerebral arteries.

## Investigation of Neuroprotective Effects of the Selective Enzyme Inhibitors Administrated During Focal Cerebral Ischemia in Rats

P 3

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### Objective

The present study was designed to investigate whether the selective inhibitor of iNOS, aminoquanidine(AG), plays a protective role in the later stage of cerebral ischemia-reperfusion.

### Methods

Wistar rats, female, weighing 220-250g were anesthetized with 6% chloral hydrate (5ml/kg body weight, i.p.). The left MCA occlusion was achieved with a nylon thread placed in the external carotid artery, through the internal carotid artery and then into the middle cerebral artery, to reach the proximal segment of the anterior cerebral artery. 3 hours later the thread were removed to allow reperfusion and received intraperitoneal injections of AG (100mg/kg twice per day). Rectal temperature of each rat was maintained at  $37.0 \pm 0.5^\circ\text{C}$  by an external lamp. Rats were randomly divided into 3 groups: (1) sham-operated group, animals subjected to the same experimental procedures as described above but the nylon monofilament was not introduced. (2) vehicle-control group. (3) AG-treated group. Rats were sacrificed at 6h, 12h, 48h, 72h or 7d after MCA occlusion. At different time points, infarct volume was determined by image analysis in TTC stained brain sections. The activity of iNOS and myeloperoxidase (MPO), the neuropathology with hematoxylin and eosin and Nissl method by light microscopy and electron microscopy were examined.

### Results

It was found that administration of AG can attenuated iNOS activity by 18.29%, 31.27%, 18.39%, 21.29%, after 12h, 24h, 48h, 72h when compared with vehicle-control groups ( $p < 0.05$ ). Also, the activity of MPO in AG groups was significantly lower than in the control groups ( $p < 0.05$ ) and AG decreased the infarct volume between the 24h and 7d groups ( $p < 0.05$ ). The abnormalities of light microscopic changes as well as ultrastructural alterations were also alleviated in AG groups.

### Conclusions

The results indicate that AG selectively inhibits iNOS activity and reduces the level of NO which contributes to severe neuronal cytotoxicity. The neuroprotective effects of AG is time-dependent

and occurs only when the drug is administered for longer than 24 hours, starting after induction of IR. The decrease of MPO activity suggests that neutrophil infiltration is involved in the pathogenesis of cerebral IR injury, a process that can be alleviated by iNOS inhibitor such as AG. These observations provide evidence that iNOS inhibitors may be useful in the treatment of ischemic stroke.

## Clinical Analysis on 65 Cases of Early Epilepsy After Spontaneous Cerebral Hemorrhage

P 4

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### Objective

To discuss the incidence, clinical features and prognosis of the early epileptic seizure within two weeks after cerebral hemorrhage.

### Method

The study and analysis on the clinical materials of 1050 cases of cerebral hemorrhage was done.

### Result

The incidence of early epilepsy after cerebral hemorrhage is 6.19%. The early epileptic seizure has close connection with the areas of bleeding (cerebral cortex and cerebral lobe)  $p < 0.01$ . Lowering of intracranial pressure with dehydration and antiepileptic treatment were effective for prevention of the early seizures after cerebral hemorrhage, but were accompanied with 27.69% of the 18.98% non-secondary epilepsy ( $p < 0.01$ ).

### Conclusion

The early epileptic seizures after cerebral hemorrhage were mostly seen at the site of bleeding, which manifested as the generalized attacks of the whole body. There were effective results after dehydration and antiepileptic treatment, but with a relatively bad clinical prognosis.

## A Randomized Controlled Clinical Trial of MgSO<sub>4</sub> Plus Cyclophosphamide and Colchicine in Patients Suffered from Acute Cerebral Infarction

P 5

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### Objective

Through randomized controlled clinical trial, we evaluated the mechanism, clinical effectiveness and safety of magnesium salt (MgSO<sub>4</sub>) plus antileukocytic drugs (cyclophosphamide and colchicine) on patients with acute cerebral infarction

### Subjects and Methods

One hundred and fifty patients were divided into 1. control group (50 Patients), 2. treatment group (50 patients) and 3. co-treatment group at random. The control group was given general therapy, the treatment group was given cyclophosphamide and colchicine in addition to general therapy, and MgSO<sub>4</sub> plus cyclophosphamide and colchicine as well general therapy were given to the co-treatment group. The neurological functional deficits were evaluated with MESSS at admission, day 30 and 90 after stroke onset. The Activity of Daily Living(ADL) was evaluated with Barthel Index(BI) at admission, day 30 and 90. Evaluation of therapeutic effectiveness was done with BI and the decrease in percentage of MESSS at day 30 and 90, respectively. The plasma level of NSE was determined at pre-treatment and post-treatment in some patients. Side effects including nausea, vomiting, leukocytopenia, flushing, infusion site pain and hepatorenal dysfunction were observed.

## Results

1. Compared with the treatment group, the decrease of neurological functional deficit scores in the co-treatment group was more obvious ( $P<0.05$ ) and the scores of BI were significantly increased ( $P<0.05$ ) at day 30. But at day 90 there was no difference ( $P>0.05$ ) between the treatment and co-treatment group;
2. The level of glucose may have effect on effect on the co-treatment, but it cannot be confirmed in this trial;
3. The decrease of plasma level of NSE in the co-treatment group was statistically significant when compared with the control group ( $P<0.01$ ) and treatment group ( $P<0.05$ ) respectively;
4. Side effects were found in twelve patients in the treatment group and in twenty-five patients in the co-treatment group. There was no hepatorenal dysfunction in these two groups.

## Conclusion

MgSO<sub>4</sub> plus cyclophosphamide and colchicine not only can reduce the neurological functional deficits, the treatment also improve the prognosis, hasten patients recovery and decrease early mortality.

The possible mechanism is magnesium and anti-leukocytic drugs act on different stages of cerebral infarction and produce significant co-effect. Side effects should be observed carefully when this therapy is used.

## A Study on the Changes in of Plasma Coagulative, Anticoagulative, Fibrinolytic Activities in Patients with Cerebral Infarction Treated with Low Molecular Weight Heparin

P 6

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### Objective

To observe the changes in plasma coagulative, anticoagulative and fibrinolytic activities parameters including prothrombin time (PT), kaolin partial thromboplastin time (KPTT), antithrombin III (ATIII), tissue plasminogen activator (tPA) and plasminogen activator inhibitors (PAI) in patients with acute cerebral infarction. To observe the effect of low molecular weight heparin (LMWH) on the parameters and to evaluate the treatment effect of LMWH.

### Subjects and Methods

Eighty cerebral infarction patients were divided into two groups. One group was given routine drug treatment and another was given LMWH treatment at the same time. Plasma PT, KPIT, ATIII, tPA, and PAI were determined before and after treatment and compared with the normal controls. Then the treatment effect of LMWH was assessed.

### Result

There was obvious decrease in KPIT ( $P<0.05$ ). ATIII and tPA activities were much higher than that before treatment. Increased in ATIII and decreased in PAI were significantly different between two groups. The therapeutic efficacy of LMWH treatment group was superior to that of the routine treatment group. No serious side effect was found.

### Conclusion

There are functional abnormalities in plasma coagulation, anticoagulation and fibrinolysis during acute cerebral infarction. LMWH may affect levels of KPIT, ATIII, tPA, PAI and regulate the equilibrium of coagulation-fibrinolysis system. The LMWH is useful and safe in therapy of acute cerebral infarction.

## 高齡急性腦血管病患者臨床診治規律探討

P 7

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### Objective

To study the clinical manifestation, treatment and prognosis of patients with age  $>80$  years old and acute cerebrovascular disease.

### Methods

150 patients aged  $>80$  years were included in our study (119 cerebral infarction and 31 cerebral hemorrhage). We studied the risk factors, clinical manifestation, complications, imaging investigation, laboratory examination, treatment and prognosis of the aged  $>80$  years group and compared with patients aged  $<65$  years.

### Results

Aged patients often presented with atypical clinical manifestations, with unconsciousness at the onset of all symptoms. They had fewer risk factors than the younger patients. The laboratory examination showed higher creatinine, BUN and blood glucose levels, low blood potassium and blood magnesium levels. Abnormal blood cholesterol and TG level were rare among aged patients.

### Conclusion

Giving specific, comprehensive treatment and proper early rehabilitation according to the clinical features of aged patients is the key to lowering of mortality and improving the quality of life in the patients with acute cerebrovascular disease.

## Relationship Between the Nco I, Ava II Polymorphism of LDL Receptor Gene and Atherosclerotic Cerebral Infarction

P 8

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### Objective

Our purpose was to investigate the relationship between the Nco I, Ava II polymorphism of LDL receptor gene (LDL-R) in patients and the occurrence of atherosclerotic cerebral infarction (ACI) among the Han nationality in Liao Ning province.

### Methods

The polymerase chain reaction (PCR) technique was used to study the polymorphisms of LDL-R gene and allele frequencies in 77 patients with ACI and 113 age-matched Chinese healthy controls. The levels of the lipid and lipoproteins were also compared among the cases with ACI and the controls.

### Results

A<sup>+</sup> frequency of LDL-R gene in healthy controls and ACI group was 0.230 and 0.125 respectively, while the N<sup>+</sup> frequencies of healthy control and ACI group was 0.667 and 0.662 respectively. In case of the coexistence of A<sup>+</sup>A<sup>-</sup> and N<sup>+</sup>N<sup>+</sup>, the Relative Risk (RR) of ACI was 4.76( $P<0.01$ ), while the RR of the increase of serum levels TG, TC, LDL-C, LP (a) was 4.29, 67.9, 3.33 and 3.09 ( $P<0.05$ ), respectively.

### Conclusion

The coexistence of A<sup>+</sup>A<sup>-</sup> and N<sup>+</sup>N<sup>+</sup> can affect the concentration of lipid and lipoprotein and was closely related to the occurrence of ACI.



## Effects of the Home-based Occupational Therapy on Motor Function of Limbs in Patients with Hemiplegia

P 9

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### Objective

To study the effects of home – based occupational therapy on motor function of limbs and independent ability of activities daily living in stroke hemiplegic patients.

### Methods

Sixty stroke patients needing hemiplegia rehabilitation program at home were randomly divided into occupational therapy group (A) and control group (B). All patients began to be treated after 16 – 25 days since onset. The general rehabilitation therapy was performed in B group, the V term training procedure of home – based occupational therapy was added to the general rehabilitation therapy in A group. All the patients were evaluated with Barthel Index and Fugle – Meyer Assessment before and after three months treatment. Then the results on independent ability of patients in activities daily living and motor function of limbs were compared in both groups.

### Results

The improvement both of Barthel Index and Fugle – Meyer in home – based occupational therapy group was much greater than that in control group ( $P < 0.001$ ).

### Conclusion

The V – term occupational therapy is a simple effective method in treatment on stroke hemiplegic and should be used widely.

### Key words

Hemiplegia; Rehabilitation; Home - based occupational; Therapy

## Clinical Significance of Blood Sugar Step-up in Acute Cerebral Infarction

P 10

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### Objective

To investigate the clinical significance of blood sugar step-up in patients with acute cerebral infarction.

### Method

Blood sugar levels were retrospectively analyzed in 89 in-patients (78 males and 11 females) with acute cerebral infarction. The mean age of these patients was 67.6 years (range 50 to 80). Sixty-one (68.53%) patients had normal blood sugar (3.70-5.90mmol/L) and 28 (31.46%) had blood sugar step-up ( $> 5.90$ mmol/L). The blood sugar level in 15 patients was 6.0-8.40mmol/L (53.57%), in 7 patients was 8.41-10.0mmol/L (25.0%), and in 6 patients was 10.0mmol/L (21.42%). According to the CT manifestation, the maximum diameter of infarct was divided into two groups: small ( $< 2$ cm) or large ( $> 2$ cm).

### Results

1) Normal blood sugar group: neurologic impairment: mild 48 (70.58%), moderate 13 (20.31%), serious 3 (4.68%). Clinical effect: Basically cured 8 (13.11%), distinctively advanced 41 (70.21%), advanced 12 (19.69%). Complication: pulmonary infection 1 (1.63%), cardiac arrhythmia 2 (3.27%). 2) Blood sugar step-up group: neurologic impairment: mild 3 (12.00%), moderate 7 (28.00%) and severe 15 (60.00%). Clinical effect: distinctively advanced 13 (46.42%), advanced 12 (42.28%), no change 2 (7.14%), worse 1 (3.57%). Complication: pulmonary infection 6 (21.42%), death 6 (21.42%). The comparison of neurologic

impairment, cerebral infarction, clinical effect, complication and death rate between normal blood sugar group and blood sugar step-up group had distinctively difference ( $P < 0.01$ ).

### Conclusion

Blood sugar level was related with cerebral infarction, neurologic impairment, clinical effect, complication and mortality. In treatment of cerebral infarction we should pay attention to the treatment of high blood sugar in time, so as to reduce the mortality and mutilation rate of cerebral infarction.

## A Study on Early Onset of Rehabilitation

P 11

### Interventions After Stroke and Factors Affecting Functional Outcome

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### Objective

To investigate the correlation between early onset of rehabilitation interventions after stroke and improved functional outcome, and factors affecting functional outcome.

### Methods

With prospective study, we observed 128 stroke patients, including 50 patients with early onset of rehabilitation interventions and 78 control patients. Several scales were used for functional measures.

### Results

In all patients, there were significant differences in the functional assessments before and after rehabilitation. Considering the difference mentioned above, there was no difference between rehabilitation group and control group, except for that assessed by Barthel index. Multiple linear regression analysis revealed that the following factors might affect functional outcome after stroke: poor cognitive function, dysphasia, and incontinence.

### Conclusion

Functional recovery occurs naturally within the first month following stroke. Poor cognitive function, dysphasia and incontinence can affect functional recovery after stroke. The effect of early onset of rehabilitation intervention needs further investigation.

### Key words

Stroke, Rehabilitation, Functional recovery

## Relationship among CT Scan and Clinical Findings in Acute Phase of Subarachnoid Haemorrhage and Subsequent Cerebral Damage

P 12

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### Objective

To search the relative factors of cerebral damage, rebleeding, delayed cerebral ischemia (DIC) and hydrocephalus after subarachnoid haemorrhage (SAH) by CT scans and clinical findings in acute phase.

### Methods

To analyze the relationship between cerebral damage after SAH and clinical findings: CT scans result, age, sex, blood pressure, hyponatraemia, therapeutic methods.

## Results

Cerebral damage was related to the pattern of distribution of SAH on brain CT and hyponatraemia. The high attack rate of rebleeding and DIC is related to presence of blood in the surface of brain, collection of blood in the ventricle, saccular aneurysms or cerebral arteriovenous malformation (AVM) ( $P < 0.01$ ).

## Conclusion

To forecast cerebral damage after SAH by study of CT scans showing and clinical findings have clinical significance. According to these findings, we may take some therapeutics to prevent the cerebral damage after SAH.

## Key words

SAH, Clinical factors, Subsequent cerebral damage, Forecast

## Surgical Treatment of Intractable Epilepsy Combining with Bipolar Coagulation on Functional Cortexes

P 13

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## Objectives

Intractable epilepsy in the area of the functional cortexes, if surgically removed, will cause the lack of neural functions. If using Multiple Subpial Transection (MST) to cure intractable epilepsy will have very good results, but have a chance of causing SAH or a scar, which will cause seizures again. We pilot to study of the resecting the epileptogenic foci combining with Bipolar Coagulation on Functional Cortexes (BCFC) to evaluate the possibility and effectiveness of using BCFC.

## Methods

124 cases with intractable epilepsy had been surgically treated in Beijing Tiantan Hospital from 1996 to 1999. 75 cases with temple lobe epilepsy underwent anterior temple lobectomy (40 cases), selective amygdalo-hippocampectomy (12 cases) or lesionectomy (23). 48 cases with extra-temple lobe epilepsy underwent lesionectomy (45) or BCFC (3). 1 case with infantile hemiplegia with intractable seizures underwent functional hemispherectomy.

All patients were examined with intraoperative electrocorticography (EcoG). If the epileptogenic foci were located and involved to the functional cortexes, such as pericentral gyrus, Broca's area and Wernicke's area, and can't be resected, combining the BCFC was used. The surface of multiple cerebral cortexes were coagulated in the bipolar output power 4 U, at intervals 5 mm apart, and duration 1-2 seconds.

## Results

There are no SAH and no lack of blood supply to the brain during operated observation. Pathological features indicated that there was coagulation necrosis in superficial layers and acute pyknosis and tissue edema adjacent to the superficial layers. The structure of deep cortex was normal. There were 4 cases showed temporary weakness on limbs strength and 5 cases aphasia and all be recovered in couple days after surgery. 64 cases were followed up after surgery 1/2-3 years. The seizure free was 80 % (51/64), the seizure attack less than 75% was 12. 5%(10/64), the seizure less 50% were 5%(4/64). The general efficiency was 97.5%.

## Conclusions

The best way is that epileptogenic foci can be removed in order cure the epilepsy, but for the epileptogenic foci involved the areas of functional cortexes, combining BCFC is useful to control the horizontal synchronization and spread of epileptic discharge.

Therefore, the BCFC is easy, safe and available for clinical apply.

## Key words

Functional cortex; Epilepsy; Bipolar-coagulation; Multiple subpial transection

## Serum and Cerebrospinal Fluid Levels of Neuron-specific Enolase in Epileptic Patients

P 14

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## Objective

To explore for neuronal damage after seizures.

## Methods

The serum and cerebrospinal fluid (CSF) levels of neuron-specific enolase (NSE) after seizures in 51 epileptic patients were dynamically determined by enzyme-linked immuno-sandwich assay.

## Results

The serum and CSF levels of NSE in epileptic patients were markedly increased after seizures. The serum levels of NSE peaked at 1<sup>st</sup> day, then decrease for about one week and returned to normal after two weeks or so. The serum and CSF levels of NSE were higher in the epileptic patients with tic or frequent seizures. There was a positive correlation between the serum NSE levels and the CSF NSE levels.

## Conclusion

NSE could be induced to reach higher levels by seizures, which suggested that neuronal damage occurred after seizures. The neuronal damage were more severe manner in cases of tic or frequent seizures. Determinations of serum NSE, instead of CSF NSE, might serve as a sensitive marker to evaluate the neuronal damage caused by seizures.

## Key words

Epilepsy, Neuronal damage, Neuron-specific Enolase

## Treating 50 Cases of Epilepsy with Embryo Tissue and Treatment According to the Different of Symptoms

P 15

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In traditional Chinese medicine, epilepsy is called "xianzheng", epilepsy has relations with the liver, spleen and kidney, the kidney stores the essence of life and blood in the liver. While the insufficiency of kidney-yin occurs the essence of life can not be turned into blood, then the blood can not nourish the liver and the brain, therefore, the marrow sea is not full and the liver-yang rises abnormally, which result in epilepsy. The incidence of the disease 0.5% or so. The expression of epilepsy is a sudden, transient, repeated disturbance of the function of the brain. The essence of epilepsy is supersynchronous discharge of nerve cell groups in cerebral cortex or subcortex. Nerve cell groups in different regions are discharging, the areas of their conduction are different, the essence of the disturbance of the function of the brain is different, the clinical manifestation is different. The most common clinical manifestation is the change and loss of consciousness, widespread or limited, tonic or paroxysmal convulsion, unusualness of sensation and behavior, changes of emotions, sensation and memory, disorder of the function of the vegetative nerve system.

1. Clinical information: Treating 50 cases of epilepsy with embryo tissue and treatment according to the differentiation of symptoms. 28 male, 22 female; 39 cases aged from 6 to 20 years old, 11 cases aged from 21 to 42; the courses ranged from 0.5 to 21 years.
2. Methods of treatment: Clean an aborted embryo coming from healthy woman with 0.9% N.S. Take it with decoction of ginseng root, prepared fleece-flower root and scorpion etc. Take half an embryo twice a day, one course includes 30 days.
3. The result of treatment: All the 50 cases are cured effectively and the result is confirmed by EEG. 12 cases have no recurrence within 5 years, 38 cases improve obviously in EEG.
4. Typical case: Chen XX, male, 15 years old, had endured epilepsy for 7 years. The boy went into convulsions after endured an injury on the head when he was 8, then be diagnosed as epilepsy, and improved after treating, but broke out interruptedly, later. The symptom had become serious before treating with the mentioned therapy. The boy acted awkwardly with low intelligence and abnormal EEG, but can ride bicycle after one course of the therapy, and his EEG became normal after two courses.
5. Discussion: Based on the mechanism for epilepsy and the theory of nourishing viscera with viscera in traditional Chinese medicine, we select embryo tissue. Overseas, it has been found that embryo tissue can promote the growth and propagation of cells and in which cells and tissue can differentiate. Therefore, embryo tissue has its internal malleability, and can produce grow-factor, promote the growth of tissues. Comparing with grown-up tissue, the antigenicity of embryo tissue is weak. The embryo tissue rarely causes immunoreaction and exclusive reaction while it can strengthen immunocompetence. Traditional Chinese medicine has an idea that epilepsy is too much trembling, slowly movement of fingers and toes, convulsions etc and that it is an expression of stirring of internal wind mainly because of wind-phlegm. The kidney is the congenital foundation, controls the bone and produces the marrow. If an embryo falls ill, the marrow sea is not full. On the other hand, when the deficiency of the liver-yin and kidney-yin occurs, yin fails to keep yang well, and the liver wind moves internally, rising abnormally with phlegm. The two situations will both result in epilepsy. Based on the theory of treatment according to the differentiation of symptoms, taking embryo tissue following its infusion adding ginseng root, prepared fleece-flower root, scorpion etc, we have conspicuous effect in treating epilepsy. Therefore, we can say that embryo tissue cause the central nerve cells to regenerate and strengthen the immunocompetence, preliminarily.

## Evaluation of the Effectiveness of Topamax in Children with West Syndrome

P 16

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### Objective

The aim of this study was to establish the efficacy, tolerability and problems associated with the use of Topamax in children with West syndrome.

### Methods

Fifteen patients with West syndrome (infantile spasms) were given Topamax, in 5 as first-line monotherapy and in 10 patients as add-on therapy to nitrazepam.

### Results

Eighty per cent (12/15) showed 100% suppression of seizures after starting therapy during hospitalization. The average dose

was 4.2mg/kg/day and the maximal dose was 7.1mg/kg/day. However, there was a high relapse rate (75%) in complete responders within the first 3 months after discharge. This was probably due to a lower maintenance dose in these patients, as those who relapsed were on an average dose of 4.2mg/kg/day at the time of relapse and responded to a stepped up dose to a maximum of 12.5mg/kg/day.

The mean duration of long-term therapy was 12 months in all the children who were followed. Three children were spasm free for 12 months.

### Conclusions

Topamax was a new agent for the treatment of West syndrome. It was well tolerated and no patients discontinued therapy because of adverse events.

## Study of Quality of Life and Memory in Adults with Epilepsy

P 17

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Epilepsy is a common chronic neurological disorder. Recurrent seizures, long term treatment of antiepileptic drugs (AEDs) and discrimination against epileptic patients made themselves and their relatives in a state of low quality of life. As a whole, the memory and intelligence of epileptic patients is impaired. As the literatures reported, there exist memory deficits in epileptic patients. More attention has been focused on the study of a new index of health—quality of life (QOL) and its influenced factors. Study about the effect of seizure attacks on learning and memory and its associated factors is an item of improving patients' quality of life. In China, there isn't any report about the study of QOL by means of epileptic specific scale in epileptic adults. In present study, an epileptic specific QOL scale was taken to evaluate the quality of life in epileptic adults, and its relationship with the memory - surveying results was also investigated. This study aims to provide some clues to further research into the quality of life in patients with epilepsy and memory, as well as to improve patients' overall quality of life and prognosis.

### Method

106 adults with epilepsy and 64 healthy people were studied and tested by using QOLIE-30 and 42 patients with GTCS and 38 healthy people were tested by using the revised Wechsler Memory Scale.

### Results

1. Compared with control groups, QOL scores were lower in epileptic patients. With worry about the seizure attacks and effects of antiepileptic medication, having memory problems, they are unsatisfied with their lives, in a blue mood, easy to be tired and their social activities are limited.
2. Comparing the QOL of patients between different sex, duration of seizure, AEDs taken and seizure frequency, we found that medication and seizure frequency take an important part. QOL is negatively associated with the number of the AEDs taken and seizure frequency.
3. The MQ of patients with GTCS was lower as compared with control group. Female and those with duration of seizure more than one year performed poorer in one subtest separately. Patients with frequent seizures accomplished worse in a few subtests.
4. MQ was associated with overall score of QOL, also with subtests of emotional well-being and cognitive function. The subtest of QOL—cognitive function was associated with many subtests of MQ.
5. Seizure frequency, educational levels, duration of seizure and the cognitive function subtest of QOL have a significant effect on MQ.

## Conclusion

1. A QOLIE-specific scale was used for the first time to evaluate the quality of life in epileptic adults in China. We found that the quality of life in epileptic patients was poor. Seizure frequency and number of AEDs were the main influencing factors. Suitable medications for seizure control was the key to improve the quality of life in epileptic patients.
2. The memory of patients with GTCS were impaired. It was associated with seizure frequency and duration of seizure. Effective control of epilepsy might improve their memory.
3. MQ was associated with emotional well-being subtest and cognitive function subtest, cognitive function subtest was associated with MQ and its subtests, may be it can represent memory to some extent.

## Cyanchum Otophyllum Crossover Trial in Refractory Partial Epilepsy

P 18

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### Objectives

Kwong Wah Hospital (KWH) and Biotechnology Research Institute (BRI) at Hong Kong University of Science and Technology (HKUST) worked in collaboration to design and conduct a clinical trial to evaluate the safety and efficacy of Cyanchum Otophyllum (CO), a Chinese Herb extract, as an adjunctive therapy in epileptic patients with refractory partial epilepsy with or without secondary generalization.

### Methods

This was a randomized double-blinded cross over clinical study, including a retrospective baseline phase and a core phase. A total of 25 patients were recruited in KWH neuromedical and neurosurgical outpatient clinical under strict inclusion and exclusion criteria. The retrospective phase was a historical assessment of seizure frequency and concomitant anti-epileptic drugs use during the four weeks prior to entry into the trial. The core phase lasted for eight months. Subjects were randomized to the two sequences of "add-on" treatment with CO or "add-on" placebo. Treatment periods lasted up to three months with a washout period of two months. A fixed dose of CO was given during the study. Patients were followed up monthly for seizure frequency, adverse events and clinical laboratory tests.

### Results

22 of 25 (88%) patients completed the trial for analysis. The medium of seizure reduction was 0.045 of the CO group compared with the placebo group. This revealed that the seizure rate in CO group was little higher than control group in terms of median statistics. The p-values of difference in seizure reduction were 0.81451 and 0.9604 by using Sign and Sign-Rank tests respectively. There was no significant advantage of CO over placebo in seizure control. Besides, only 4 of 22 patients after taking CO had a seizure reduction rate at least 50%. Thus 18% of subjects were responders. No major adverse event was recorded in all patients.

### Conclusions

We found that CO did not show any statistically significant reduction in seizure rate as an adjunctive therapy of refractory partial epilepsy with or without secondary generalization. However, the safety profile of the drug was good as no major adverse event was recorded. The study was partially restricted by the inadequate number of patients recruited. We suggested that a further large study was needed to document the usefulness of CO in epileptic patients.

## Utility of the Electronencephalogram in Clinical Practice

P 19

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### Background

The EEG detects abnormalities in cerebral function; its diagnostic value is highest in situations with rapid progression, affecting midline diencephalic and mesencephalic structures. We looked at the clinical utility of the EEG in clinical practice.

### Methods

We reviewed all consecutive requests for a routine scalp EEG over eight months. The setting was the electrodiagnostic centre of a teaching hospital. The indications were recorded as well as the factual and clinical reports. The results of the EEG were classified into three groups: a) definite abnormality such as inter-ictal epileptiform discharges; b) non-specific or borderline abnormality such as frontal intermittent rhythmic delta activity and c) normal. The referral patterns that emerged and the EEG findings for each of the main referral category were recorded.

### Results

801 EEGs were requested during this period. The clinical indications for EEG could be categorised into seven groups. Cases were referred if 1) patients had paroxysmal symptoms that could have been due to epilepsy ie. syncope, dizziness (33%); 2) patients were diagnosed with psychiatric disorders such as schizophrenia, depression; 3) patients were already diagnosed with epilepsy (21%); 4) patients presented with infection of the nervous system (6%); 5) patients had known intracranial pathology such as acute hydrocephalus or intracerebral haemorrhage (3%); 6) patients had headache (1%) and 7) patients had a number of heterogeneous illnesses such as dementia, decline in cognitive function (13%). The percentage of abnormal and borderline EEGs respectively for each category were as follows: 1) Paroxysmal disorders: 13%, 25%, 2) Psychiatric disorders: 0.5%, 14%, 3) Epilepsy: 46%, 22%, 4) CNS Infection 79%, 6%, 5) Intracranial pathology: 4%, 30%, 6) Headache 0%, 12.5% and 7) Miscellaneous 15%, 11%.

### Conclusion

The likelihood of abnormalities on a first EEG for patients with epilepsy was 46%; another 22% had non-specific findings. EEGs from patients with headache and psychiatric illnesses have a poor detection rate; the indication for routine recordings in these two situations should be scrutinised.

## A Case Series of Frontotemporal Lobar Degeneration

P 20

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We present a case series of 4 male patients with Frontotemporal Dementia (FTD), diagnosed in 2000-01, who gave a history of insidious onset of decline in social interpersonal conduct, and loss of insight into their problems at work during their late 40's and 50's of age. These included instilling diesel instead of petroleum of motor cars, aggression towards children, driving the wrong routes as a taxi driver, and speaking foul language to customers as a herbalist shop-keeper. Poor awareness of personal hygiene and conduct became obvious early in the course of illness in 3 patients. Hyperorality and stereotypic behaviour was prominent in 3 patients. Carbohydrate craving and picca was reported in 2 patients respectively. At the time of diagnosis at our center, the patients were aged 60, 71, 69 and 71 respectively, when speech impairment was severe in all cases; demonstrating mutism, echolalia and perseveration. 2 patients made

singing utterances. CT Scan of brain all showed marked frontal and temporal atrophy, with frontal index at 46.3, 44.6, 43.8, and 22.2 respectively. 1 patient was labeled with schizophrenia previously. A family history of psychological disorders was obtained in one patient. 3 patients were still community dwelling with family members, and 1 was admitted to our infirmary ward. 2 patients showed improved behaviour on SSRI. Another patient M/69 with previous diagnoses of stroke and parkinsonism. A review of history and physical findings, with paucity of vascular risks and absence of absence of response to L-dopa; plus prominence of asymmetrical limb akinesia and dystonia, together with marked grasp reflex of hands led to a diagnosis of Corticobasal Degeneration (CBD). His neurocognitive profile showed a frontal pattern of impairment. Videos of the psychomotor phenomenon of all patients will be shown. The relationship between FTD and CBD in neuropathology and clinical presentation will be discussed.

## Social Activities, Life Events and Alzheimer's Disease

P 21

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### Purpose

To evaluate the etiologic association between social activities, life events and Alzheimer's disease (AD).

### Methods

An age, sex, educational level, 1:1 matched case control study was conducted in Beijing, Shanghai, Chengdu, and Xian. 282 cases and 282 controls were drawn from a prevalence study of dementia in elderly population in these cities. The risk of AD related to social activities and life events were fitted to conditional Logistic model.

### Results

Individuals participating some kind of activities when they aged 40 years or over, may have reduced risk to suffer from AD. The activities were as follow. First, to plant flower, to keep birds or small animal. Second, to play card, mahjong, or chess. Third, to watch TV, movie or live show. Fourth, to read or write. Individuals ever suffered from some kind of great negative life events may have increased risk to suffer from AD. The life events were as follow. First, to experience the death of spouse or children. Second, to enrolled in lawsuit or put in prison. Third, to suffered from occupation failure or lose one's job. Fourth, to attend war. The adjusted OR of AD in individuals attended these four kinds of activities for 1 to 9 years was 0.647 (95%CI: 0.513 to 0.817), 10 to 19 years was 0.419 (95%CI: 0.263 to 0.667), 20 years and more was 0.271 (95%CI: 0.135 to 0.545) compared with individuals not participated these activities. The risk of AD increased to 2.256 fold (95%CI: 1.257 to 4.050) in every increased kind of negative life event.

### Conclusions

The study demonstrated that attending activities may have protective effect to AD, suffering from great negative life events may be a risk factor for AD.

## Abnormal Neuroglial Proliferation in Hippocampus of Patients with Alzheimer's Disease

P 22

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### Objective

To investigate the distribution of gliocytes in hippocampus of patients with Alzheimer's disease (AD) and its possible roles in the process of AD.

## Methods

The splices of hippocampus from 3 cases of AD and 2 normal controls were stained with Bielschowski's staining and Holzer's staining respectively.

## Results

The classic pathological changes including senile plaque (SP) and neurofilament tangle (NFT) were seen. We observed, at the same time, that numerous astrocytes and microglia cell bodies whose processes crossed each other were present near that focal lesion. Contrasted with reactive glial proliferation, the number of neurons in hippocampus of AD cases was significantly low.

## Conclusion

Chronic inflammation exists in AD brain. Our observation stresses the importance of gliocytes in process of AD, and support the recent hypotheses that chronic inflammation may play a key pathogenetic role in AD.

### Key words

Alzheimer's disease; Hippocampus; Gliocytes

## The Ratios of $\beta$ -amyloid Precursor Protein Isoforms in Platelets from Senile Dementia Patients and its Significance of Diagnosis

P 23

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### Objectives

To detect the expression of  $\beta$ -amyloid precursor protein (APP) in the elements of peripheral whole blood, to analyze the platelet APP isoforms and their levels and to study whether a differential level of platelet APP isoforms is specifically related to Alzheimer's disease (AD) and whether it can be considered a peripherally diagnostic index.

### Methods

The expression of APP in peripheral blood cells was determined by immunohistochemical analysis, and the levels of APP isoforms were evaluated by means of western blot analysis in platelets from 20 patients with AD (10 mild, 6 moderate and 4 severe), 10 patients with non-Alzheimer's-type dementia (NATD), 15 patients with non-dementia of other neurological disease (NDND) and 15 normal controls (NC).

### Results

1. In peripheral whole blood, platelets were APP strong immunoreactivity, lymphocytes were APP weak immunoreactivity, and other whole blood cellular elements were not immunoreactivity.
2. Five APP isoforms (90kd, 95kd, 100-110kd, 120-130kd and 140-150kd) are present in platelet and the molecular weight ranges from 90kd to 150kd.
3. The ratios of the intensity of the 120-to-130kd APP isoform to the 140-to-150kd.
4. APP isoform, and the 120-to-130kd APP isoform to the 100-to-110kd APP isoform were significantly lower in the AD and mild AD groups ( $P < 0.05$ ), as compared with NC, NDND and NATD groups.
5. Both ratios of platelet APP isoforms positively correlated with the scores of neuropsychological tests in AD group ( $r = 0.464$  to  $0.603$ ,  $P < 0.05$  or  $0.01$ ), and negatively correlated with age in NC, NDND and NATD groups ( $r = -0.407$  to  $-0.614$ ,  $P < 0.05$  or  $0.01$ ).

### Conclusions

1. Platelet is the major source of circulating APP and  $A\beta$ .
2. The lower ratios of platelet APP isoforms can be considered

an early marker for AD, allowing for discrimination between AD and other types of dementia.

#### Key words

Alzheimer's disease, Dementia, Platelet, Amyloid precursor protein

## Study of the Prophylactic and Curative Effect on Vascular Dementia and its Mechanisms of Cerebellar Fastigial Nucleus Electrical Stimulation in Rats

P 24

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### Objectives

To investigate the effect of prevention and treatment on vascular dementia (VD) and its possible mechanisms of cerebellar fastigial nucleus electrical stimulation (FNS).

### Methods

The animal model of vascular dementia was established in rat by repeated occlusion of both carotid arteries in combination with hypotension. The electrodes were implanted into bilateral cerebellar fastigial nucleus. Rectangular pulses with intensity of current 70-75mA, frequency 50Hz, duration 0.5ms were adapted for FNS. FNS persisting for 1-hour was given once 2 days before repetitive global cerebral ischemia/ reperfusion (I/R), and once a day immediately and 11 weeks after repetitive I/R for 7 days. The effect of FNS and its possible mechanisms were assessed by behaviour tests, neuropathology, and the expressions of Bcl-2 mRNA, 5-HT, cyclic AMP response element binding protein (CREB) and phosphorylated CREB (p-CREB).

### Results

1. FNS significantly improved the capacity of cognition in rats with VD ( $P<0.01$ ), when it was given 2 days before repetitive I/R and immediately and 11 weeks after repetitive I/R.
2. FNS evidently reduced the neuronal cell loss in hippocampus ( $CA_1$  throughout  $CA_4$ ) and neocortex in rats ( $P<0.01$ ), when it was given before and immediately after repetitive I/R.
3. After FNS, the expression of Bcl-2 mRNA, 5-HT and p-CREB were up-regulation ( $P<0.05$  or  $0.01$ ).

### Conclusions

FNS may be benefit to the prevention and treatment of VD in rats and the up-regulation of the expressions of Bcl-2 mRNA, 5-HT and phospho-CREB may contribute to it.

#### Key words

Vascular dementia; Electrical stimulation; Fastigial nucleus

## Prevalence of Peripheral Vascular Disease in Patients with Ischaemic Stroke

P 25

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### Objectives

Patients with ischaemic stroke have a higher likelihood of coronary artery and peripheral vascular disease. The prevalence of co-existing peripheral arterial disease in patients with stroke has not been evaluated comprehensively and is a further indicator of the severity of the atherosclerotic burden in these subjects. This cross-sectional study was performed to determine the prevalence of co-existing

peripheral arterial disease in patients with ischaemic stroke at the University of Malaya Medical Centre (UMMC), Kuala Lumpur.

### Methods

55 consecutive patients with ischaemic cerebral infarction or transient ischaemic attack were recruited from May to July 2001 from the neurology outpatient clinic and the general medical wards. Demographic and clinical information including symptoms of intermittent claudication and conventional stroke risk factors were obtained. Patients with recurrent strokes were excluded from the study. A portable hand held Duplex ultrasound machine was used for peripheral vascular assessment. Ankle:brachial blood pressure index was calculated and subjects were diagnosed to have existing peripheral arterial disease when the index is less than 0.9.

### Results

24% ( $n=13$ ) of patients with ischaemic stroke within our study group had peripheral vascular disease. Most of these patients (77%;  $n=10$ ) were asymptomatic and only 3 had intermittent claudication. Those with peripheral vascular disease were significantly older (mean 69.6 yrs vs 61.8 yrs) and were more likely to suffer from concurrent diabetes, hypertension, hyperlipidaemia and to be smokers.

### Conclusions

Peripheral vascular disease is common in patients with ischaemic stroke but not usually evaluated. It is more likely to be present in those with concomitant conventional risk factors. Ankle:brachial blood pressure index is a useful adjunct to clinical assessment to determine the overall atherosclerotic burden.

## Screening for Cognitive Impairment in Acute Stroke Patients

P 26

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### Objectives

To investigate a) the prevalence of cognitive impairment and dementia in patients admitted for acute stroke; b) the sensitivity and specificity of screening instruments in such patients.

### Methods

All patients admitted with acute stroke to the Department of Neurology were screened with the Mini Mental State Examination (MMSE) and the Elderly Cognitive Assessment Questionnaire (ECAQ) if they were not dysphasic, comatose or non-resident. Patients with scores of MMSE  $<26$  or ECAQ  $<8$  were further investigated with repeat assessments at 6 weeks post-stroke. Dementia was diagnosed using DSM-IV criteria.

### Results

319 patients were admitted for acute stroke over 3 months. Of these, 74 (23%) were excluded, mainly because of dysphasia. Of the 245 eligible patients, 68 (28%) were not assessed because of early discharge and 41 (17%) were not assessed because of language barriers or failure to obtain consent. 47 (19%) were found to be cognitively intact. 35 of the remaining 89 patients were diagnosed with dementia (86% vascular, 8% Alzheimer's Disease and 6% mixed) after repeat assessments. Logistic regression analysis showed that only MMSE at screening was a significant predictor for dementia ( $p=0.001$ ). The sensitivity and specificity of a MMSE cut-off of 21 was 93% (95% CI 82-98%) and 87% (95% CI 79-92%) respectively.

### Conclusions

This study shows a 14% prevalence of dementia in patients eligible for this study. However, this figure may be an underestimate as dysphasic patients were excluded and many patients were not assessed. A cutoff score of 21 on the MMSE

was determined to be sensitive and specific for screening purposes in hospitalised acute stroke patients. Further studies are required to investigate the factors leading to cognitive impairment and dementia after stroke.

## Hypodensity of >1/3 MCA Territory Versus Alberta Stroke Programme Early CT Score (Aspects): Comparison of Two Methods of Quantitative Evaluation of Early CT Changes in Acute Ischaemic Stroke in the Community Setting P 27

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### Objectives

To evaluate the accuracy and reliability of two commonly used methods of detecting significant early computed tomography (CT) ischaemic changes in hyperacute stroke patients.

### Methods

All patients admitted to a community hospital in Hong Kong during the year 2000 with a diagnosis of suspected acute ischaemic stroke and a CT brain scan performed within 6 hours of symptom onset were recruited. There were 175 patients, 95 were excluded (62 with intracranial haemorrhages, 25 with inconclusive findings, & 8 with poor scan quality), the remaining 80 patients comprised the study cohort i.e. confirmed acute ischaemic stroke (45%), transient ischaemic attack/TIA (34%) and non-stroke conditions (21 %). Three blinded observers (one neurologist and two radiologists) given minimal history (eg. side of weakness) independently evaluated the scans using two scoring methods: (1) ATLANTIS/CT Summit Criteria to determine  $\leq$  or  $>$  1/3 MCA territory involvement, (2) ASPECTS  $>$  or  $\leq$  7. The trial radiologist, with full knowledge of all clinical and radio-logical information, evaluated the scans separately and served as the gold standard.

### Results

(1) The gold standard determined that 9/80 scans (11.25 %) showed  $>$  1/3 MCA territory involvement, and 15/80 scans (18.75 %) had an ASPECTS  $\leq$  7. (2) For determination of  $\leq$  versus  $>$  1/3 MCA territory involvement, all 3 observers agreed in 69 cases (86 %), with a (moderate) inter-rater reliability ( $\kappa = 0.52$ ,  $SE \pm 0.13$ ). Average sensitivity and specificity were 48.11 % and 94.98 %, respectively. (3) For determination of ASPECT  $>$  versus  $\leq$  7, all 3 observers agreed in 40 cases (50 %), with a slight inter-rater reliability ( $\kappa = 0.15$ ,  $SE \pm 0.13$ ). Average sensitivity and specificity were 60 % and 82.56 %, respectively.

### Conclusions

(1) When the prevalence of extensive early CT ischaemic changes was low (10-20 %), both the  $>$  1/3 MCA territory involvement criteria and ASPECTS were associated with inadequate accuracy and reliability. (2) In contrast to a previous report, the  $>$  1/3 MCA territory involvement criteria was more specific and reliable compared to ASPECTS.

## Cerebral Ischemia and cGMP Producing Cells in the Gerbil Hippocampus P 28

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To observe cerebral ischemia and cGMP producing cells in the gerbil hippocampus. Both vessels occlusion and immunofluorescent methods in gerbils hippocampal tissue slices were used. The results showed that cerebral ischemia increased cGMP synthesis in the CA<sub>1-3</sub>

subfields. cGMP positive cells distributed mainly in CA<sub>1</sub> subfield. Most of cGMP positive cells are astrocytes. The number of small round cGMP positive cells was increased after recirculation following ischemia in the dentate gyrus. These results indicate that cerebral ischemia increased cGMP synthesis in the CA<sub>1-3</sub> subfield. Most of cGMP positive cells were astrocytes. It is possible that astrocytes may play an important role in the regulation of metabolism in the early ischemic reperfusion state.

### Key words

Cerebral ischemia, Hippocampus, cGMP, Astrocytes, Immunohistochemistry

## The Clinical Significance and the Test of Estradiol and Testosterone in Male Patients with Cerebral Infarction P 29

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### Objective

To investigate the clinical significance and the changes of estradiol (E2) and testosterone (T) in male patients with cerebral infarction.

### Methods

By RIA test, the levels of serum E2 and T were dynamic observed in 62 male patients with cerebral infarction. To analyze the relationship between the changes of E2, T and the religion of the infarction, size of the infarction, stage and condition.

### Results

1. The serum E2 concentrations were increased and T concentrations were decreased in acute stage of the male cerebral infarction patients, which had remarkable difference from those of the control group ( $P < 0.01$ ). The serum E2 and T returned to normal level in the convalescent stage. It was no significant difference.
2. During the acute stage of the patients, the levels of serum E2 and T in patients with subcortex infarction were significantly lower than those of cortex infarction ( $P < 0.05$ ).
3. During the acute stage of the patients, the levels of serum E2 in patients with large size infarction were lower than those of small size infarction ( $P < 0.05$ ). However the change of serum T is no significant difference. 4. The levels of serum E2 and T in patients with severe cerebral infarction were lower than those of mild cerebral infarction in acute stage ( $P < 0.05$ ).

### Conclusion

The levels of sex hormone (E2, T) in the male patients with cerebral infarction were disturbance. There is remarkable relationship between the changes of E2, T and the religion of the infarction, size of infarction, stage and prognosis.

### Key words

Cerebral, Infarction, E2, T, male

## The Study and Clinical Significance of the Relationship Between Anticardiolipin Antibodies and Stroke P 30

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### Objective

To explore the clinical significance of the relationship between anti-cardiolipin antibodies and stroke.

## Methods

In this study, the positive rate of ACA in plasma of 104 patients with cerebral infarction, 27 with TIA, 41 with cerebral blood flow deficiency, 33 with cerebral hemorrhage, and 100 normal subjects were evaluated by ELISA methods.

## Results

The positive rate of ACA in patients with cerebral infarction is highly significant statistically ( $p < 0.01$ ). We conclude that Ig G type ACA has some clinical value with these patients. Also, we noticed that ACA positive is more relevant to stroke in young adults and the incidence of multi-infarction is more common on ACA positive Stroke.

## Conclusions

ACA can act as an indicator of an increased severity of cerebral infarction.

## Key words

Anti-cardiolipin antibodies; Strokes; ELISA; Cerebral infarction

## The Relation Among the FV Leiden Mutation, the Anticardiolipin Antibodies and Ischaemic Cerebrovascular Disease P 31

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## Objective

To study the incidence of resistance to activated protein C (APC-R) caused by an Arg506 Gln mutation in the factor V gene in Chinese population and ischaemic cerebrovascular disease (ICVD) patients, the DNA analysis and the clotting tests, which measure the degree of prolongation of plasma clotting both in the presence and in the absence of APC, were used as the laboratory diagnostic method.

## Method

The factor V Leiden mutation was analyzed in 75 healthy control and 118 ICVD patients. The anticardiolipin antibodies (aCL) level was also measured by enzyme-linked immunosorbent assay (ELISA) with international standards in 86 patients with ICVD. Genomic DNA from whole blood was used to amplify part of the factor V gene by polymerase chain reaction. The G to A mutation at codon 506 was detected using the restriction enzyme Mnl I (PCR-RFLP analysis) followed by polyacrylamide gel electrophoresis.

## Results

The mutation, in heterozygous form, was found in 6 cases out of 118 ICVD patients, with a incidence of 5.1%, with no statistical significance in comparison with the normal controls ( $P > 0.05$ ). None of the 75 healthy control were found to carry the FV Leiden mutation. The difference in FV Leiden mutation between patients and controls was not significant ( $P > 0.05$ ). In 86 patients whose aCL level was also measured simultaneously, elevated aCL level were found in 26 cases.

Three of the 26 cases with elevated aCL were found to carry the FV Leiden mutation, making the group of patient possess a incidence of 11.5%, showing no strong statistical significance in contrast to the patients without elevated aCL 5%. However, 3 of 6 cases of FV Leiden mutation found in this group were patients with elevated aCL.

## Conclusion

This study found 5.1% FV Leiden mutation in 118 Chinese patients of ICVD. 11.5% cases with elevated aCL carried FV Leiden mutation. Three of 6 cases of FV Leiden mutation were patients with elevated aCL. The final combined analysis

revealed FV Leiden mutation is of highly significant relation to aCL in this group of Chinese patients with ICVD. It also present the first 3 Chinese cases of FV Leiden mutation combined higher aCL level, namely hereditary APC resistant Gln506-FV.

It suggested that although FV Leiden mutation accounted for a small proportion of patients with ICVD, it plays a crucial role in thrombosis. Its detection is of great clinical significance in finding cause, predicting the progress, prevention and treatment. Further studies may lead a new way to treat patients with ICVD.

## Depression Associated with Acute Cerebral Stroke P 32

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## Aim

To investigate early diagnosis and anti-depression treatment for the Depression Associated with acute cerebral Stroke (DAS) and its effect on the function recover after stroke.

## Method

20 cases of DAS were classified into two groups, 12 cases of which were treated with anti-depression agent and eight of which were not treated with anti-depression agent. The difference in their clinical manifestation and radiological image were compared between the two groups.

## Result

The difference in symptom relief and function recovering between the two groups is significant.

## Conclusion

Depression is a common associated disorder after acute stroke and early diagnosis and proper management are important for their future recovering and improvement of their quality of life.

## Key words

Depression; Acute; Cerebral; Stroke

## Recent Infection and Acute Cerebral Infarction in Senile Patients P 33

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In this article, 160 patients with recent infection associated with acute cerebral infarction were analyzed, among which there were 94 males and 66 females whose average age was 68.54 years. There were 115 cases of respiratory tract infection, 19 cases of urinary tract infection, 8 cases of intestinal tract infection 8 cases of biliary tract infection, 3 cases of intracranial infection, 3 cases of feet and skin infection and 4 cases of unknown reason.

The average duration before the cerebral infarction was 10 days. There are many risk factors of cerebral infarction which include hypertension, diabetes, obesity, smoking, coronary heart disease and hyperlipidemia. But there is no confirmed conclusion that whether the recent infection is a main cause of cerebral infarction.

The mechanisms that cause cerebral infarction may include: (1) Infection may cause the activation of monocyte and macrophage which can promote the activity of prothrombinkinase and cause the hyperfunction of coagulation. (2) Infection may raise the level of TNF and other factors in peripheral blood and can change the coagulation function of endothelial cell of blood vessel and increase the activity of



adhesion molecules of the endothelial cells. (3) The level of fibrinogen of the patients with recent infection may be higher and can cause the coagulation-promoting state of the body.

## Home-based Rehabilitation Services for Stroke Patients

P 34

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### Purpose

To exam the effectiveness of the seamless, multi-disciplinary home-based rehabilitation services for the stroke patients discharged from an acute ward in United Christian Hospital (UCH).

### Background

As the district hospital in Kowloon East, UCH takes care a great amount of stroke patients from the district. In 1999-2000, there were around 900 strokes cases registered in UCH with an average of 5 days in each stay. To be more effective in the management of stroke, we adopted the multi-disciplinary approach in different phases, i.e. acute, rehabilitation and community phases.

The weekly ward round conducted in the acute phase enhances the inter-disciplinary communication and ensures the appropriate management of every stroke patient. For the community phase, a home-based rehabilitation services was started since November 2000. With the goals to facilitate timely and safe discharge; and returning the patients to community, the objectives of the home-based rehabilitation services are going to:

- Improve patients' functional status
- Improve patients' mobility level
- Improve the well-being of patients and the carers

### Methods

Patients for the study were selected through the weekly ward round in an acute ward. The selection criteria are as follows:

- Patients with principal diagnosis of acute stroke, either first or recurrent
- Patients discharged from hospital to home directly

Different outcome measures were adopted to assess the differences in functional status (Barthel Index), Mobility level (Elderly Mobility Scale), Quality of life (SF-12), patient's satisfactory and carer's stress.

### Results

Since November 2000 till April 2001, 69 stroke patients received our home-based rehabilitation services. Totally 139 visits were provided for these patients. The mean in BI was improved from 78.4 to 86.1 with  $P < 0.05$ . For SF-12, both physical and mental scores showed significant improvement with  $P < 0.05$ . Besides, carer of those patients received our home-based rehabilitation also demonstrated less stress and more confidence in taking care of the patients.

The mean carer stress questionnaire showed the decrease of stress from 48.7 to 40.7 with  $P < 0.05$  as well. Lastly, it was appreciated that all the patients and their relatives were satisfied about the services.

### Conclusions

The home-based Rehabilitation Services was an effective method to improve the functional status, mobility level, well-beings of stroke patients discharged from acute wards. Their carers will also benefit with being less stress and are more confident in caring the patients.

## A Study on the Relationship Between Serum Estradiol and Regional Cerebral Blood Flow in the Male Vascular Dementia Patients

P 35

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### Objective

To investigate relation of male vascular dementia with the levels of sex hormone and regional cerebral blood flow.

### Methods

The changes of Estradiol, Progesterone, PRL, FSH, LH and testosterone were determined with radioactive immunity analysis method in 41 cases male vascular dementia patients. rCBF were determined by <sup>133</sup>Xe inhalative method.

### Results

1. The E<sub>2</sub> in the cerebral infarction patients with dementia and the cerebral infarction patients without dementia were reduced compared with that of control. The E<sub>2</sub> in the cerebral infarction patient with dementia was much more reduced than the cerebral infarction patients without dementia. The Prog, PRL, FSH, LH, T of the two groups showed no difference from that of control.
2. The rCBF in the cerebral infarction patients with dementia and the cerebral infarction patients without dementia were reduced than that of control, the rCBF in the cerebral infarction patients with dementia was much more reduced than the cerebral infarction patients without dementia.

### Conclusion

Results suggested that the reduced level of E<sub>2</sub> can lead to the reduction of rCBF, and it can lead to the increase of vascular dementia.

### Key words

Vascular dementia; Estradiol; Regional cerebral blood flow; Cerebral infarction

## The Symptoms and Prognosis of Central Nervous System Involvement in Systemic Lupus Erythematosus

P 36

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### Objective

To investigate the symptoms and prognosis of systemic lupus erythematosus (SLE) with central nervous system (CNS) involvement.

### Methods

The clinical data of 93 SLE patients with CNS involvement were retrospectively reviewed in our hospital.

### Results

- 1) The symptoms were classified as diffuse manifestations (51.6%), focal manifestations (23.7%), seizures (24.7%) and headache (10.8%). The most common symptoms were psychosis (32.3%), seizure (24.7%), stroke (20.4%) and altered consciousness (17.2%).
- 2) The prognosis of focal manifestations was significantly worse than that of diffuse manifestations (mortality rate 36.4% vs 10.4%, cure rate 18.2% vs 62.5%,  $P < 0.05$ ). Seizures had the similar prognosis with diffuse manifestations (cure rate 69.6% vs 62.5%,  $p = 0.61$ ). The prognosis of strokes is the worst (mortality rate 42.1%, cure rate 21.1%) than other symptoms ( $P < 0.01$ ).

3) The other two factors associated with poor prognosis were elevated cerebrospinal fluid protein and  $\leq 2$  years' SLE duration at CNS involvement.

### Conclusion

The distribution of CNS symptoms in SLE was similar with the overseas reports. The prognosis was significantly related to clinical features in CNS.

## The Clinical Research of Imaging of Dopamine Transporter in Distinguishing Essential Tremor and Early Parkinson's Disease

P 37

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### Objectives

To evaluate the value of  $^{99m}\text{Tc}$ -TRODAT-1 SPECT dopamine transporter (DAT) imaging for differencing early Parkinson's Disease (PD) from essential tremor (ET) and study the clinical relationship between the ET and PD.

### Methods

Nine patients with ET, fourteen patients with early PD, five patients with the combination of ET and PD (ET-PD) and twenty age sex-matched healthy subjects were studied by  $^{99m}\text{Tc}$ -TRODAT-1 SPECT DAT imaging. Striatum specific uptake of  $^{99m}\text{Tc}$ -TRODAT-1 was calculated according to the ratio of striatum (ST) and cerebellum (CB).

### Results

In the patients with early PD, the means ( $\pm$ SD) of the bilateral ST/CB ratios (left:  $1.46 \pm 0.21$ ; right:  $1.38 \pm 0.16$ ) were significantly lower than the mean of the bilateral ST/CB ratios of the age gender-matched control subjects (left:  $1.78 \pm 0.15$ ; right:  $1.80 \pm 0.14$ ) ( $P < 0.01$ ). The mean of the bilateral ST/CB ratios of the patients with ET (left:  $1.69 \pm 0.13$ ; right:  $1.72 \pm 0.14$ ) was comparable with that of the age gender-matched control subjects (left:  $1.75 \pm 0.12$ ; right:  $1.74 \pm 0.11$ ). The mean ( $\pm$ SD) of the bilateral ST/CB ratios of the patients with ET-PD (left:  $1.41 \pm 0.10$ ; right:  $1.37 \pm 0.05$ ) were significantly lower than the mean of the bilateral ST/CB ratios of the age gender-matched control subjects (left:  $1.82 \pm 0.20$ ; right:  $1.74 \pm 0.11$ ) ( $P < 0.01$ ).

### Conclusions

$^{99m}\text{Tc}$ -TRODAT-1 SPECT DAT imaging can help us to difference early PD from ET. It was considered that PD and ET had been different disease entities.

## 33 Patients of Facial Spasm Treated by TOPAMAX

P 38

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### Objective

To study the clinical effects of facial spasm patients treated by TOPAMAX.

### Method

62 patients of facial spasm were divided into two groups in random. 33 patients were in treatment group others were controls, the treatment group patients were divided into 4 classes by the disease course and severity, the treatment group patients were treated by TOPAMAX, the priming dose of TOPAMAX was 25 mg or 50 mg bid. Cumulated to effective dose, raising 25 mg a week, after the facial spasm symptom disappeared followed a two-week treatment. The controls treated by Phenytoin Sodium with does 0.1 tid.

### Result

Patients (classes 0-1) with facial spasm symptom disappearing treated by TOPAMAX. Reached 64% of all, Patients (class 4) reached 12% of all, after two week's treatment. Patients (classes 0-1) reached 88% of all; Patients (class 4) reached 6% of all after 8 weeks' treatment. Controls: Patients (classes 0-1) with facial spasm symptom disappearing reached 10% of all, patients (class 4) reached 52% of all after 2 weeks' treatment, Patients (classes 0-1) reached 31% of all, Patients (class 4) reached 38% of all. There is an obvious difference between two groups ( $P < 0.05$ ).

### Conclusion

TOPAMAX, when used to treated facial spasm, is effective and has few side effects.

### Key words

TOPAMAX (TPM), Facial Spasm

## The Deletion Analysis of Parkin Gene Exon 2-5 on Early Onset and Later Onset Parkinson's Disease

P 39

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### Objective

To investigate distribution of deletions in the parkin gene among patients of early onset and later onset Parkinson's disease in China, and to explore whether parkin gene played important role in the pathogenesis of variant types of Parkinson's disease.

### Method

53 patients were divided into early onset ( $< 50$ y) and later onset ( $> 50$ y) groups. Exon 2-5 were amplified by PCR with the template of genomic DNAs of patients. Deletions distribution were observed by 1% agarose electrophoresis, and the clinical characteristics was then analyzed.

### Results

Among all of the 53 cases, exon 2 and exon 4 was deleted in 1 patient separately, exon 3 deletions were found in 2 cases; whereas exon 5 deletion hasn't been found in either group. All of those deletion existed patients are belonging to the group of early onset Parkinson's disease.

### Conclusions

There was relatively high incidence of parkin deletions in Chinese patients of Parkinson's diseases with the initiate age exceeded 30 years old, it suggested that parkin exon deletions contributes to early onset Parkinson's disease in China.

### Key words

Parkinson's disease, Parkin gene, Deletive mutation

## To Discuss the Relationship of the Clinical and Complement C3 with Tourette Syndrome

P 40

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### Objective

The paper reports the clinical data for eighty patients suffering from Tourette syndrome (TS) and the phenomenon for reduced the complement C<sub>3</sub>. To discuss the relation to the etiology.

## Method

In the TS and non-TS group, the abnormal rate of reduced complement C<sub>3</sub> are compared by the Chi-Square test.

## Result

In the TS group, the abnormal rate of reduced complement C<sub>3</sub> was 37.8 per cent and in the non-TS group the abnormal rate of reduced complement was 15.4 percent. The abnormal rate of reduced complement C<sub>3</sub> between the group  $\chi^2=3.932$ ,  $P<0.047$ , there is significant difference.

## Conclusion

This study reveals that reduced complement C3 in the TS group is a specializing factor with TS immunity or with immunology etiology.

## Key words

Tourette Syndrome, Complement C3, Etiology, Clinical, Relationship

## A Specific 25kD Protein Component Deficiency in Skeletal Muscles of Myasthenia Gravis P 41

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## Objectives

To explore whether the 25 kD protein component was a specific decrease in skeletal muscles of myasthenia gravis (MG).

## Methods

Skeletal muscular proteins were extracted from 21 cases of healthy subjects, 18 cases of MG and 20 cases of other neuromuscular disorders (ONMD) with Gubstraub solution. At meantime, muscular proteins from 18 cases of healthy subjects, 21 cases of MG and 23 cases of ONMD were also extracted with PBS. Components of protein were analyzed by SDS-PAGE in double blind method.

Density of the 25 kD protein bands was counted by Bio-electrophoresis Image Scanner. Isoelectric point and molecular attribution of the 25 kD protein were demonstrated by two-dimensional electrophoresis and FITC conjugated ConA staining, respectively.

## Results

In the experiment of muscular proteins extracted by Gubstraub solution, density value for the 25 kD protein bands was  $1.61\pm0.66$  in the MG muscles, but was  $3.43\pm1.54$  and  $3.72\pm1.52$  in the muscles of normal and ONMD, respectively. In the muscular proteins extracted by PBS, the protein density value was  $1.22\pm0.45$ ,  $3.95\pm1.65$  and  $4.13\pm1.05$  in the muscles of MG, normal and ONMD, respectively.

Two-dimensional electrophoretic analysis demonstrated that the 25 kD protein band displayed in the SDS-PAGE consisted of two major protein components, besides there were almost similar protein components in the muscular proteins extracted with PBS and Gubstraub solution. In addition, the 25 kD protein was found to be a glycoprotein.

## Conclusions

The decrease of 25 kD glycoprotein had a fair specificity in the skeletal muscles of MG, therefore, it was suggested that the development of the MG muscle weakness and/or the pathogenesis of the MG could be associated with lack of this functional protein.

## Clinical, Electrophysiological and Pathological Observation on Hereditary Motor and Sensory Neuropathy

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## Objective

To study the clinical electrophysiological and pathological features in hereditary motor and sensory neuropathy (HMSN).

## Methods

Clinical symptoms and signs, electromyography (EMG) and pathology of sural nerve biopsy were analyzed in 27 patients with hereditary motor and sensory neuropathy from 3 families.

## Results

The initial age of this group was between 5-16 year old. The typical manifestations were symmetrical weakness and atrophy in the distal limbs, with depressed or absent of ankle reflexes and foot sagging. Among which all patients also suffered from atrophy in their distal upper limbs. Additionally, upper limbs hyperreflexia (12/27), positive Hoffmann sign (12/27), and pes cavus (10/27) were noted. Electrophysiological study revealed that conduction velocity of motor nerves was reduced. Histopathological examination of peripheral nerves showed demyelination. Among all patients, 5 have malformation of fingers, suggesting there is a linkage between this malformation and HSMN, and the gene is probably near the chromosome 17p<sup>11.2-12</sup>.

## Juvenile Muscular Atrophy of Distal Upper Extremity (Hirayama Disease) P 43

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The article summarizes 13 cases of juvenile muscular atrophy of distal upper extremity (Hirayama disease) to study its features clinically, electromyographically (EMG) and histologically by muscular biopsies. Hirayama disease is characterized by an initially progressive muscular weakness and wasting of the distal upper limbs in youngster (15-30 years) followed by spontaneous arrest within several (2-3) years, no inducement, unilaterally or bilaterally involvement, predominantly in men. EMG show denervation, motor unit lost, fasciculation and fibrillation potentials, lengthened motor conduction time, attenuated amplitude but normal motor and sensory nerve conduction. Most changes exist on affected side, but subclinical electrophysiological abnormalities may be seen on the non-atrophic side, which suggest that the lesion likely exists in the anterior horn of spinal cord at lower cervical and upper thoracic levels. Muscular pathology indicate neurogenic muscular atrophy. The atrophy in the disease occurred in a random pattern and there may be a serious lesion in adjacent normal or mildly abnormal tissues. There is no apparent difference in the degree of atrophy in the same case. Group phenomenon is over 80% and target fiber is scarce. Secondary myopathic change may also be seen. We detect the SMN exogene VII/VIII in 4 patients whose onset age is accordance to that of SMA (2-17 years). No deletion is found. The pathogenetic mechanism seems to be related with circulatory insufficiency in the local spinal cord. Hirayama disease may be a subtype of cervical spinal disease.

## Key words

Juvenile muscular atrophy, Clinic, EMG, Pathology

## Peripheral Nerves Injury of Electrophysiological and Pathology in MS

P 44

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### Objective

We report the EMG and pathological features of sural nerve biopsy of 12 patients with MS. The pathological of these 11 patients demonstrated demyelination injury of peripheral nerves.

### Methods

Twelve cases anomaly are screened with EMG from 60 cases MS. Sural nerve biopsy were analyzed by HE AND loyez, and electron microscopy.

### Results

EMG showed slow of MCV in 9 patients and SCV in 7 patients. Myelinated fibres was the presence in 8 sural nerve biopsy patients and most striking demyelinating fibres, regeneration of myelinated fibres.

### Conclusion

MS is characterized by demyelinating disorder limited to the CNS. There are, however, the results of this study suggested that combine with PNS demyelinating injury in MS may be more frequent than is generally assumed.

## The Difference of Clinical Feature Between Chinese and Japanese with Poems Syndrome

P 45

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POEMS Syndrome, also defined as Crow-Fukase syndrome, is a multisystem disorder syndrome characterized by polyneuropathy. The first two cases were described in 1956, by Crow. In 1968, the cases were regarded as a unique syndrome by Fukase. In 1987, this syndrome was first reported in China. Since then, increasing number of cases were reported. In order to enhance our understanding, we investigated the clinical features of POEMS syndrome between Chinese and Japanese patients. A total of 94 cases reported in China including two from our hospital were reviewed and compared with 102 cases from Japan. Although, the multiple clinical manifestations were similar between Chinese and Japanese, some specific features such as splenomegaly, lymphadenopathy, mild fever, hyperhidrosis, M protein were different. Race difference might lead to higher incidence of splenomegaly and lower incidence of lymphadenopathy in Chinese, in contrast to that of Japanese patients. Furthermore, Durpo examination have been used extensively in later 80's which might be responsible for the finding rate. Since immunoelectrophoresis has lower detection rate than immunofixation in M protein determination, it may explain the difference.

## Detection of Deletions of the DMD Gene by Reverse Dot-blotting Hybridization with the Cloned Exon Probes

P 46

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### Aim

Preparation of probes used to detect the major deletion-prone exons of DMD gene, and doing a feasibility study by reverse dot-blotting with them.

### Methods

Human genomic DNA was extracted from peripheral venous leukocytes of healthy people. Using PCR technique, 18 nucleic acid fragments were amplified. The fragments was extracted from 2% agarose gel, and then connected with pGEM-T Easy vector. The recombinants were transformed into E.coli JM109 competent cells, followed by being planted in Amp<sup>r</sup>LB culture medium and being cultured. The positive clones were selected. The fragments were completely released by Not I-digestion of recombinants. The specificity of these fragments used as probes was detected by reverse dot-blotting hybridization assay with a patient of DMD and a healthy people.

### Results

The cloned fragments were high consistent with several exons of the DMD gene. The hybridization results were coincidental with the results of PCR identification.

### Conclusion

The cloned probes are specific and suitable for the identification of clinical DMD gene deletion diagnoses.

### Key words

Probes; Hybridization; DMD; Gene deletions

## Preliminary Clinical Observations on Effect of Brevisapin on Type 2 Diabetic Polyneuropathy

P 47

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### Objective

To investigate the effect of brevisapin on diabetic polyneuropathy.

### Methods

Sixty seven patients with diabetic polyneuropathy were involved in a randomized positive-control clinical trial. 37 cases were treated with brevisapin injection solution 20 ml (containing total flavone 90mg) intravenous infusion daily for 2 weeks; 30 cases were treated with cytidine diphosphate choline in same way and served as controls. All patients were also administered VitB6, nimodipine at the same time and the original diabetic treatments were carried on. All patients' limb spontaneous pain, limb numbness, great toe vibration sense, ankle reflexion, major common peroneal nerve conduction velocity were evaluated in pre and post therapy by tow neuropathic attending physicians.

### Results

Spontaneous pain and numbness of limb were improved by 96% and 97% in brevisapin group, which were much higher than those in controls (56% and 60% respectively). Great toe vibration sense, ankle reflexion, major common peroneal nerve conduction velocity showed better response in brevisapin group than in controls (95% vs 47%, 93% vs 52%, 86% vs 20% respectively). Brevisapin also benefited limb coldness, constipation and vision illness to a certain extent. No obvious side effects were found.

### Conclusion

Brevisapin is worthy of use a safe effective agent in the treatment of diabetic polyneuropathy.

## Retinal Vascular Complications of Facioscapulohumeral Muscular Dystrophy (FSH)

P 48

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### Objectives

Retinal exudates, clinically indistinguishable from those which occur in Coats' Disease, are a rare and treatable complication of

FSH, and underlying asymptomatic retinal telangiectasis is detectable by fluorescein angiography in most FSH patients (as reported from The Institute of Ophthalmology, Moorfields Eye Hospital and the National Hospital for Neurology and Neurosurgery (see RB Fitzsimons, EB Gurwin and AC Bird, *Brain* 1987,110, 631-648). It is presently aimed to obtain a global and longitudinal perspective on this association in order to consolidate policy on screening FSH patients for visual complications.

## Methods

Data on retinal complications of FSH was obtained from (i) follow-up of personal cases previously reported, as above (ii) patients referred via the US FSH Society (iii) survey of the literature.

## Results

Retinal exudates treatable with Laser photocoagulation frequently antedated the onset of obvious or serious muscle disease, especially in young children, or otherwise occurred early in the disease. Late detection of retinal exudates may lead to irreversible visual loss. Although retinal telangiectasis occurs in most FSH families, some families seem particularly at risk of overt visual complication.

## Conclusion

Treatable retinal exudates are rare in FSH, but are nevertheless sufficiently common to justify ophthalmological surveillance, especially when the disease presents in childhood, when overt retinal disease may antedate serious muscle manifestations.

There may be some racial variation in the incidence of FSH. FSH has sometimes been thought not to occur or to occur very rarely in ethnic Chinese. Nevertheless, cases from Taiwan and the PRC are now being reported, and it may prove to be as common in Chinese as in Caucasians. Chinese physicians should be aware of retinal complications, and of the importance of early detection and treatment, and wherever possible visual complications of FSH should be reported.

## OTHER ABSTRACTS

### Observation of Intracranial Artery Occlusive Diseases in Hypertension Diabetes Mellitus Patients

OA

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## Objectives

To investigate frequencies of intracranial artery occlusive diseases in hypertension (HT) and diabetes mellitus (DM) patients and risk factors of HT and DM to cerebral artery stenosis.

## Methods

We retrospectively assessed 845 patients (Group 1  $\geq 50$  years old, mean age  $60.1 \pm 8.0$  years; Group2  $< 50$  years old, mean age  $38.7 \pm 8.2$  years) who visited the Department of Neurology of the First Affiliated Hospital of Zhejiang University, and 2325 patients (mean age,  $59.8 \pm 9.1$  years) who visited the Department of Neurology of the Peking Union Medical College Hospital. All the patients underwent transcranial Doppler detection. We evaluated stenotic and occlusive lesions of MCA, ACA, PCA, BA and VA. Age, sex, hypertension (HT) and diabetes mellitus (DM) were included in the analysis.

## Results

Among the patients not younger than 50 years old, the frequencies of MCA stenosis were: South 6.96%, 11.43%, 20.59% and 1.75%; North 6.24%, 11.18%, 13.51% and 1.95% respectively, when suffering from HT, DM, both of HT and DM, or neither of them.  $\chi^2$  tests showed that HT and DM were significantly correlated with

cerebral artery lesions ( $p < 0.05$ ) and the risk ratios of HT, DM, both of HT and DM are: South 4.0, 6.5 and 11.8; North 3.2, 5.7 and 6.9; and combining from South and North 2.9, 16.9 and 37.3 respectively. The frequencies of each stenotic or occlusive artery lesions under HT, DM and HT&DM diseases were similar between the South and North ( $p > 0.05$ ). Multiple logistic regression analysis showed that HT and DM were significant and independent predictors for MCA stenotic lesions.

## Conclusions

Hypertension and diabetes mellitus may contribute to the development of stenotic and occlusive lesions of the cerebral arteries in Chinese people.

### The Angular Gyrus Syndrome: A Specific Pattern of Neuro-cognitive Impairments after Stroke

OA

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## Objectives

To assess the type and severity of neuro-cognitive deficits after ischaemic strokes involving the Left Angular Gyrus in a local Chinese population.

## Methods

Four patients with a clinical diagnosis of Angular Gyrus syndrome (AGS) from Jan 1998 to Jun 2001 were reviewed. Their clinical presentation, neuro-cognitive deficits in terms of memory, performance on cognitive tests, language functions, praxis, calculation and right-left orientation were analyzed, together with their profiles outlined individually, both before and after cognitive remediation training.

## Results

There were two male and two female patients with a mean age of 74.5 years (71-80), two had left parietal infarct, and two had left temporo-occipital infarct on CT scan. One had mild right hemiparesis and another one had right homonymous hemianopia. Mean modified Barthel Index on admission was 90.5 (81-100).

The results of the cognitive assessments are shown in the following table.

Table 1: Initial assessment results on admission and repeated assessment results on discharge (i.e. 2-4 weeks later, after cognitive remediation training and speech therapy offered)

Assessment results on admission/on discharge				
Patient	A	B	C	D
Memory	NA / -	- / -	+ / +	+ / +
Praxis	- / -	- / -	- / -	- / -
Writing	+ / -	+ / +	+ / +	+ / -
Language Comprehension	+ / +	+ / +	+ / +	+ / -
Language Expression	+ / +	+ / +	+ / +	+ / +
Calculation	+ / +	NA / +	NA / NA	NA / +
Left-Right Disorientation	+ / -	NA / -	- / -	- / -
Visuospatial	+ / +	NA / +	+ / +	- / -

Notes: NA – Not amenable to testing; + : deficit present; - : no deficit noted

Cognitive remediation training offered include errorless learning and paired associate learning. On the language aspect, the most consistent finding among these patients is dysphasia of the conduction type, with phonemic paraphasia being the most prominent feature. Speech therapy targeted on different cueing and monitoring of verbal responses.

## Conclusions

The Angular Gyrus syndrome can cause different degrees of neuro-cognitive impairments, notably in terms of writing, language comprehension and expression in our series, which may show some

early improvement after cognitive remediation training. Cautions have to be exercised to delineate the specific language difficulties, and to differentiate the condition from other types of dysphasia as well as dementia.

## The Research of Dopamine Transporter Imaging of Patients with Parkinson's Disease OA

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### Objectives

The first purpose of this study was to evaluate the value of  $^{99m}\text{Tc}$ -TRODAT<sub>1</sub> SPECT DAT imaging for early diagnosing PD. Second, we studied the relationship between the severity of PD and the changes of DAT concentrations in striatum.

### Methods

Twenty-three patients with PD and eighteen healthy subjects were studied by  $^{99m}\text{Tc}$ -TRODAT<sub>1</sub> SPECT DAT Imaging. Striatum specific uptake of  $^{99m}\text{Tc}$ -TRODAT<sub>1</sub> was calculated according to the ratio of striatum (ST) and cerebellum (CB). All patients with PD were scored on the UPDRS and Hoehn-Yahr stages.

### Results

In the hemi-Parkinson's disease group, the DAT specific uptake of  $^{99m}\text{Tc}$ -TRODAT<sub>1</sub> was significantly lower ( $P < 0.01$ ) in contralateral ( $1.32 \pm 0.03$ ) than in ipsilateral striatum ( $1.36 \pm 0.04$ ) to the clinically symptomatic side. There was significant reduction ( $P < 0.01$ ) of striatum DAT uptake in patients with hemi-PD (LST:  $1.35 \pm 0.04$ ; RST:  $1.33 \pm 0.04$ ) compared to the age gender-matched controls (LST:  $1.37 \pm 0.05$ ; RST:  $1.36 \pm 0.04$ ). Significant negative correlations were found between scores of total UPDRS, activities of Daily Living, Motor examination and the ST/CB ratio of  $^{99m}\text{Tc}$ -TRODAT<sub>1</sub> uptake. There was not correlation between the ST/CB ratio and the score of Mentation Behavior and Mood.

### Conclusions

The results demonstrated that  $^{99m}\text{Tc}$ -TRODAT<sub>1</sub> SPECT DAT imaging can not only help us to confirm the diagnosis of PD at the early stage, but also assess the severity of PD.

## Cognitive Performance After Stroke: Preliminary Findings in a Longitudinal Study of Singapore Patients OA

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### Objectives

To investigate the cognitive performance of stroke patients.

### Methods

The Vascular Dementia Battery (VDB) was offered to patients recruited for the European & Australasian Stroke Prevention in Reversible Ischaemia (ESPRIT) trial at baseline (within six months post stroke) and annually thereafter. Patients with dysphasia or disabling stroke (Rankin  $> 2$ ) were excluded. The VDB assesses six cognitive domains: attention, language fluency, verbal memory, visual memory, visuoconstruction and visuomotor speed. Dementia was diagnosed using DSM IV criteria. Those who did not meet the DSM IV criteria but were impaired in one or more cognitive domains were classified as 'cognitively impaired but not demented'.

### Results

Of the 208 patients recruited into ESPRIT to date, 12 were not assessed because of exclusion criteria and lack of consent.

Demographics of the 196 assessed patients were (mean  $\pm$  SD): age =  $60.5 \pm 10.8$ , education =  $5.0 \pm 4.0$  years and gender = 66% male. At baseline, 55% of patients were not demented, 41% were 'cognitively impaired but not demented' and 4% were demented. Of the 96 patients who were eligible for a 1-year follow-up assessment, 21 either died or were lost to follow-up.

Preliminary findings on the 75 patients who were reassessed reveal that 83 % had the same classification as at baseline: 5% remained 'demented', 57% 'not demented' and 20% 'cognitively impaired but not demented'. Of the 17% who had a changed classification, 12% improved from 'cognitively impaired but not demented' to 'not demented', 4% deteriorated from 'not demented' to 'cognitively impaired but not demented' and 1% deteriorated from 'cognitively impaired but not demented' to 'demented'.

### Conclusions

This study suggests that long-term cognitive performance in stroke patients may alter. Further studies are needed to investigate the causes of this change.

## Cognitive Performance and Dementia After Acute Stroke OA

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### Objectives

To investigate cognitive performance following acute stroke in patients admitted early to hospital.

### Methods

The Vascular Dementia Battery (VDB) was offered to patients recruited into an acute stroke trial with a 12 hours time window (Intravenous Magnesium Efficacy in Stroke – IMAGES trial) 3 months or more after randomisation. Patients with dysphasia were excluded. The VDB assesses six cognitive domains: attention, language fluency, verbal memory, visual memory, visuoconstruction and visuomotor speed. Dementia was diagnosed using DSM IV criteria. Those who did not meet the DSM IV criteria but were impaired in one or more cognitive domains were classified as 'cognitively impaired but not demented'.

### Results

Of 120 eligible patients recruited into IMAGES over a 24 months period, 95 were assessed. Patient demographics were: age =  $63.33 \pm 12.24$  (mean  $\pm$  SD), gender = 52.6% male, ethnicity = 74% Chinese, 15% Malay & 11% Indian. 51% were not demented, 40% were 'cognitively impaired but not demented' and 9% were demented. Binary logistic regression showed that only age was an independent predictor for cognitive impairment.

### Conclusion

In this group of patients admitted within 12 hours of stroke ictus, the incidence of dementia was lower than that of cognitive impairment without dementia. Further studies are required to identify risk factors for, the natural history and treatment of cognitive impairment after stroke.

## Syringomyelia: Peculiar Presentations OA

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### Objectives

Tracing uncommon and different presentations of syringomyelia.

## Methods

Full history and clinical examination of five syringomyelic cases are correlated with MR of the spinal cord.

## Results

Four cases were type 11 (idiopathic): The first was seen by an orthopedician for an elbow charcot joint and ulnar nerve entrapment (cervical and dorsal syrinx), two cases presented by progressive motor weakness of both lower limbs (extensive dorsal syrinx) while the fourth presented by chronic occipital headache and upper backache (cervical syrinx). The fifth (type 1), associating Chiari malformation, presented by long-standing left-sided clumsiness (posterior column and pyramidal) and recent hoarse voice (vocal cord paralysis).

## Conclusion

Syringomyelia has a wide range of presentations other than a mere brachial amyotrophy and sensory loss and its first announcement might not be at the neurologist office.

## Atypical Presentation of Guillain-Barré Syndrome – Report of 2 Cases

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### Background

Guillain-Barré syndrome (GBS) is an acquired demyelinating polyneuropathy which typically present with progressive, generalized weakness and hyporeflexia or areflexia. Many variants exist but most shared a common feature - hyporeflexia or areflexia. However, we described 2 patients whom we believe had GBS but with preserved/slightly brisk reflexes and electrophysiological changes of predominantly distal motor conduction block.

### Case Report

**Case 1:** A 34 year old woman developed cervical and lumbar back pain one week after a viral illness, followed by numbness of hands and feet as well as mild weakness of both upper and lower limbs one week after onset of symptoms. The symptoms improved over the ensuing week. 2 weeks after the onset of symptoms, she developed right facial weakness which after 3 days involved the other side as well. Examination 2 weeks after onset of symptoms demonstrated severe lower motor bifacial weakness, normal extremity power and normal sensation. Reflexes, however, were slightly brisk. Electrophysiological studies demonstrated prolonged motor distal latencies of medial, ulnar, tibial and peroneal nerves, normal motor nerve conduction velocities and no conduction block. F wave and sensory conduction were normal. The needle examination did not reveal any abnormalities. Cerebrospinal fluid (CSF) demonstrated 0 WBC/mm<sup>3</sup>, protein 96 mg/dL, and normal glucose. The bifacial weakness improved gradually over 3 months.

**Case 2:** A 37 year old man developed lower backache with bilateral calf pain 2 weeks after an episode of gastroenteritis. 2-3 days after the onset of symptoms, he developed progressive weakness of hands and feet. Examination after 1 week of symptoms demonstrated symmetrical distal muscle weakness sparing the proximal muscles. Sensation was normal. Reflexes, however, were brisk. Electrophysiological studies were normal in the upper limbs. In the lower limbs, it was remarkable for prolonged tibial & peroneal distal motor latencies, small amplitude tibial and peroneal compound muscle action potentials. Partial conduction block was demonstrated distal to the fibular head. Needle examination revealed reduced recruitment and denervation changes in distal lower limb muscles. Cerebrospinal fluid demonstrated 0 WBC/mm<sup>3</sup>, protein 75 mg/dL, and normal glucose. The weakness fully recovered after 2 months.

## Conclusions

Both patients had clinical, electrophysiological and CSF features suggestive of GBS except preserved/slightly brisk reflexes. In both cases, the diagnosis of GBS was not considered in view of preserved reflexes until electrophysiological studies and CSF results were available. We believe these cases could represent variants of GBS with atypical presentation.

## The Clinical Application Research of AEEG Monitoring in Diagnosis of Epilepsy

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### Objective

To study the practical diagnostic value of AEEG monitoring on the patients with epilepsy.

### Methods

The AEEGs and clinical data were analyzed retrospectively in 80 patients with epilepsy and abnormal AEEG.

### Results

1. AEEG showed widespread abnormalities in 44 patients and focal abnormality in 36 patients. The abnormal EEG localized on the left temporal, right temporal, occipital, frontal and central regions in 10, 14, 6, 4 and 2 patients respectively.
2. The EEGs showed very high voltage paroxysmal slow wave (26 cases), runs of spike and slow wave complexes (42 cases), runs of spike or sharp waves (15 cases), diffuse spike or sharp waves (12 cases).
3. 24 patients showed abnormal AEEG in both awakefulness and sleep. 8 patients displayed abnormal AEEG in all stages of NREM sleep and REM sleep. 55 patients displayed abnormal AEEG in stage I, II, III of NREM sleep.
4. 12 patients with psychomotor seizures showed epileptic discharges in the temporal region. The abnormal EEG localized at the left temporo-central in patients with AVM. The focus of EEG coincided with the findings at operation.

### Conclusions

AEEG could detect focal abnormality with localization value in the patients with clinical generalized seizures. The detection rate of epileptiform discharges during sleep was higher than during awakefulness. The epileptiform discharges mainly appeared in stages I, II, III of NREM sleep.

## The Clinical Effect of Middle Cervical Ganglion Block Therapy in Patients with Pertinacious Insomnia

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The purpose of this study was to observe the clinical effects of middle cervical ganglion block (MCGB) therapy in patients with pertinacious insomnia (PI). 12 patients with PI (2 males and 10 females) with average age  $52.42 \pm 12.04$  years were recruited into this study. These patients all underwent MCGB daily in two sides by turns (7 injections). Injections were made near the transverse process of C6. Treatment effect was assessed after two weeks and two months. The sleep time after therapy (two weeks:  $5.23 \pm 1.52$ h,  $5.19 \pm 1.54$ h) was significantly higher than that in pre-therapy ( $2.61 \pm 0.88$ h,  $p < 0.01$ ). The mechanism is probably that MCGB regulate the secretion of melatonin, and correct patient's physiology rhythm turbulence. This minimally invasive sympathectomy technique would inaugurate a new method to the treatment of insomnia.

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### 提要

通過化驗來說明腦梗塞患者CGRP較正常人減少，ET較正常人增高，經消栓靈治療後ET較治療前減少，CGRP較治療前增高。

### 關鍵詞

腦梗塞、消栓靈CGRP ET

降鈣素基因相關肽CGRP是一種由37個氨基酸構成的生物活性多肽，廣泛存在於心血管擴張、心肌正性變力、變時作用。抑制脂質過氧化，保護多種組織細胞。對心血管系統的生理起著重要調節作用<sup>1</sup>。同時研究表明絕大部分存在於神經系統的內皮素卻有極強的縮血管作用，是一種促損傷因素<sup>2</sup>，那麼腦梗塞病人CGRP和ET含量和健康人有何差別？我們做了如下試驗。

### 材料方法

觀察對象：我們把經頭顱CT檢查證實有腦梗塞的患者作為觀察對象，其中男33人，女23人，平均年齡 $60.396 \pm 9.0$ ，其中高血壓患者12人，平均血壓為 $147 \pm 26.4/89.29 \pm 11.75$ mmHg，同時把同年齡段各項化驗指標均正常的25人做為對照組。

抽血方法：給腦梗塞患者每日靜點消栓靈3支，共21天，在治療前後空腹抽血2ml放入-20°C冰箱保存待查。

方法和試驗：用中國人民解放軍總醫院東亞免疫技術研究所提供的超微量放射免疫試驗盒，消栓靈由北京京航制藥廠生產。批准文號：京衛藥準字(90)第217號。

### 結果

表一：

	例數	ET	CGRP
腦梗塞	56	$132.64 \pm 37.84$	$43.23 \pm 17.76$
健康者	25	$54.08 \pm 8.3$	$55.53 \pm 0.7$
P值		<0.001	<0.001

表二：腦梗塞患者治療前後的ET和CGRP變化

	ET	CGRP
治療前	$132.64 \pm 37.84$	$43.23 \pm 17.76$
治療後	$72.92 \pm 23.67$	$78.75 \pm 21.37$
P值	<0.001	<0.001

### 結論

ET主要存在於神經系統的血管內皮細胞<sup>3</sup>，ET與受體結合不依賴Ca<sup>++</sup>存在。鈣的拮抗劑、血管加壓素及其他拮抗劑也不能與ET受體結合<sup>2</sup>。其縮血管效應比去甲腎上腺素強1000倍，比AT-II強10倍<sup>4</sup>，且缺O<sub>2</sub>引起ET合成與其釋放，成為病變的惡性循環<sup>5</sup>，當機體缺O<sub>2</sub>可引起CGRP保護因子減少，抑制ET能力減弱，從而發病，根據動物實驗和我們對病人的觀察，可以得出如下結論。

1. 消栓靈能使損傷因子ET減少，可能因為消栓靈與ET結構相同<sup>2</sup>，競爭ET受體，因而減少了ET損傷。同時CGRP升高，改變了機體缺O<sub>2</sub>狀態，也是ET減少的原因。
2. 兩者不相關，說明它們來源於不同系統，但是又是相互作用、相互調節。同時對機體健康有主要影響的兩種物質。
3. 有人發現高血壓患者ET增高，ET縮血管作用很強，ET又是腦血管病原因之一，缺O<sub>2</sub>又能使ET增高，故測量ET，可說明機體缺O<sub>2</sub>程度。對預防腦血管病有主要意思。
4. CGRP為人體保護因子，能抑制ET的釋放，將來隨科學發展，CGRP用於臨床無疑是一個大的突破。
5. 有人試驗培增普利、硝酸甘油、昇丙腎能使ET下降，故此類藥物可防治腦血管病。

## Clinical Observation on Sibelium Treating Vertigo Caused by Vertebrobasilar Insufficiency

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### Objective

To observe the clinical efficacy of sibelium treating vertigo caused by vertebrobasilar insufficiency (VBI).

### Methods

90 cases were divided randomly into treatment group (n=60), which was treated with oral sibelium and control group (n=30), which was treated with intravenous tetramethylpyrazine. The groups were also treated with the same basic therapy. After four weeks, the clinical efficacy was compared between the two groups and TCD was re-examined.

### Results

The total effective rates were 93.3% and 63.3% in treatment group and control group respectively, the therapeutic efficacy of treatment group was obviously superior to control group (p<0.01).

### Conclusions

The therapeutic efficacy of sibelium treating vertigo caused by VBI is obvious. Therefore, it is a first choice drug.

## Clinical Significance of Delayed Cerebral Edema Following Cerebral Haemorrhage

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### Objective

To study the clinical significance and the duration of cerebral edema following cerebral haemorrhage.

### Methods

46 patients with delayed cerebral edema were follow-up by CT scan and compared with control group.

### Results

The low density shadow plague surrounding the haemorrhagic focus was larger and cerebral edema was more severe than that at onset after day 21 in 46 patients. The clinical features were confusion, intermittent headache, vomiting, but no progression of limb paralysis.

### Conclusions

The time of cerebral edema was variable and in some patients it exceed three weeks. We should use dehydration therapy in suitable patients to decrease the complications arisen.

### Key words

Haemorrhage of the brain, Cerebral edema, Delayed absorption

## Study of Clinical Application and Production of Parkin's Capsule (Pill)

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### Objective

Parkin Capsule (pill) is Mao Dou extract whose effective single body element is Levodopa, combined with several traditional



Chinese medical herb such as Panax, Gynostema Pentaphyllum, Polygonum Multiflorum, Radix natoginseng, Magnolia Officinalis etc. This task is about the production and clinic application of Parkin Capsule (pill).

## Methods

Study on pharmacodynamics and acute toxicity of Parkin Capsule (pill) was completed in older mice. The clinic study was conducted according to UPDRS (Unified Parkinson's Disease Rating Scale) and WEBSTER SCORE, the study observed the improvement of clinic features and balance of DA and Ach, abnormal increase of activity of MAO-B, elimination of free radical, excitatory amino acid toxicity to the nerves and change of the immunity, blood lipid, hemorheology, cerebral circulation. The analysis of therapeutic effect between the Parkin Capsule (pill) and Sinemet was studied comparatively.

## Result

The study shows that Parkin Capsule (pill) has the efficiency of cultivating liver and kidney, invigorating spleen and resolving phlegm, enriching qi and nourishing blood. It can ameliorate obviously the clinical features, such as tremor, hypokinesia, rigidity and abnormal gait and posture, it can also resist and defend oxidation and protect nerve, total effective rate is 83.28%.

## Conclusions

Parkin Capsule (pill) can restore the dopaminergic and cholinergic physiological balance in the striatum by enhancing significantly the dopamine, simultaneously raising the Ach by lowering the activity of cholinesterase, which is different from the traditional treatment. This idea start the new way about the drug treatment for PD. These data suggest Parkin Capsule (Pill) has reliable efficacy and has little side effects. So it is one of the preparations for the treatment of Parkinsonism and it can be widely used in the clinics.

## 中西醫結合治療腰椎間盤突出膨出症102例臨床探討 OA

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### 摘要

探討中西醫結合治療腰椎間盤突出、膨出症的臨床效果。方法：骶管注射、中藥治療。結果及結論：102例椎間盤突出、膨出症：一療程治癒83例。顯效11例、有效3例；二療程顯效3例，有效1例。總有效率100%，遠期療效十分滿意。

### 關鍵詞

椎間盤突出、膨出症、骶管療法、中藥治療

## The Study on Vertebrobasilar Ischemic Vertigo Checked with Coloured Doppler OA

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### Objective

To study the practical diagnosis value of coloured doppler to evaluate vertebrobasilar ischaemic vertigo (VBIV).

### Methods

60 cases with VBIV were evaluated with coloured doppler about each morphologic constitution and hemodynamics. Finally, the vertebrobasilar inner space stenosis, blood stream velocity decrease, external resistance increase were found.

### Conclusion

The coloured doppler checkup is a important method to evaluate VBIV about its pathogenesis diagnosis.

## 以面神經麻痺為首發及主要表現的吉蘭-巴雷綜合症一例報導 OA

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患者，男，23歲。因加側閉目無力，口角左偏8小時以“面神經炎”於2000年12月30日收住院。之前1月內無明確感冒及腹瀉史，也無耳部受涼、吹冷風史。

查體示右側周圍性面神經麻痺症外，餘無異常，予地塞米松、針灸、理療等處理，3周後好轉出院。出院後4天無誘因再次出現右眼閉目無力、口角左偏，左眼閉目亦稍差，左側鼻唇溝變淺，鼓腮試驗兩側均差，以右側為重，於2001年1月28日再次入院治療。查體示雙側周圍性面癱症外，尚見雙上肢肌張力稍低，四肢腱反射均未引出，雙肘、膝關節以下痛覺稍減退，巴氏症（一），1月31日查肌電圖示F波未引出，所檢周圍神經傳導速度減慢，波幅減低，提示神經根、髓鞘、軸索不同程度的損害。2月1日腦脊液蛋白2033.00mg/L，IgG 224.00mg/L，IgA 32.30mg/L，IgM 16.4mg/L，細胞數  $2 \times 10^6/L$ ，頭顱MRI未見異常，診為“吉蘭-巴雷綜合症”。經神經營養藥物、改善微循環等治療，患者病情漸好轉。3周後復查肌電圖亦有明顯好轉，1月後痊癒出院。

### 討論

吉蘭-巴雷綜合症 (Guillain-Barre Syndrome, GBS) 又稱為急性感染性多發性神經根神經炎，是臨床上急性弛緩癱瘓的常見原因之一。依其電生理和神經病理表現，可分為以脫髓鞘病變為主的急性炎性脫髓鞘型GBS (AIDP) 和以神經軸索型GBS (AMAN) 和急性運動感覺性軸索型GBS (AMSAN)。AMAN僅有運動神經軸索受累，AMSAN運動和感覺神經軸均受累。

此外，臨床上GBS還有許多變異型。本例以一側面神經麻痺起病，早期易誤診為“面神經炎”，隨著病程的進展，漸表現為雙側面神經麻痺為主的徵象，結合其他體徵、肌電圖及腦脊液改變，符合GBS的診斷標準。由此作者推想，部份以面神經麻痺為首發及主要表現的病人，可能最後應診斷為GBS，必要時可行肌電圖、腦脊液等輔助檢查以確診。

## 天眩清治療動脈粥樣硬化性椎基動脈系統供血不足隨機抽樣研究 OA

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### 摘要

為探討天眩清注射液(天麻素注射液)對動脈粥樣硬化性椎基動脈供血不足的療效。

### 方法

對符合條件的病例用 Richid 隨機抽樣的方法將病人隨機分配到治療組或對照組。治療組用天眩清注射液 600mg 靜點，對照組用維腦絡通靜點，觀察10天。

### 結果

治療組與對照組相比，療效非常顯著( $p < 0.001$ )。並可使血黏度降低，BAEP顯著改善，MDA下降，SOD升高。

### 結論

經本組研究證明天眩清注射液是治療椎基動脈供血不足的安全有效的藥物。

### 關鍵詞

椎基動脈供血不足、天眩清注射液

## Study of Correlation Between Times of a Disease and Plasma Fibrinogen Molecular Reactivity in Patients with Acute Cerebral Infarction

OA

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### Purpose

To explore correlation among times of cerebral infarction and fibrinogen molecular reactivity in plasma, clinical factor in the patients with cerebral infarction.

**Methods:** The fibrin monomer polymerization velocity (FMPV), fibrinogen (Fg), ODmax and FMPV/ODmax were measured in 143 patients with acute cerebral infarction (ACI) in six hours, the 143 ones were divided at randomly into two groups, 70 ones of no-thrombolytic therapy (NTT) and 63 ones of thrombolytic therapy (TT) group. We also selected 31 cases with TIA and 30 cases with cerebral infarction history in past 6 months as contrast group. The length, weight of wet and dry of external thrombosis model and some clinical indexes in samples were also measured at same time.

### Results

The length of external thrombosis model at UACT group compared with ACI group were no significant difference at six hours ( $p>0.05$ ) and were found to be raised remarkably at 12 hours ( $p<0.01$ ), the other times the length in UACI group were higher than ACI group; the moist weight were no difference at six hours ( $p>0.05$ ) and were found to be raised remarkably at 24 hours and the fifth days ( $p<0.01$ ), at the other times, the results were no difference; FMPV were significant difference from 12 hours to 120 hours and were no difference at the other time, FMPV were significant difference among four groups ( $p<0.01$ ), the UACI group was remarkably higher than TIA group ( $p<0.01$ ). Fg raised in ACI as compared with TIA and DCG ( $p<0.01$ ). Fg was no difference at 12 and 24 hours ( $p>0.05$ ), and was raised from third days. FMPV/ODmax were found to be raised at 24 hours, 72 hours and 168 hours ( $p<0.05$ ). BPC adhibit ratio was difference at 12 hour between two groups ( $p<0.05$ ). One was no difference in other times between two groups ( $p>0.05$ ). The peak of BPC adhibit ratio in UACI group was at 24 hours and reduced with thrombolytic treatment, but one was raised 120 hours again. It indicated that the systolic pressure at administration, and the length of external thrombosis in the patients of thrombolytic treatment or no one were found to have influence on FMPV by multivariate regression analysis. Wet weight and hypertension history were found to have significant influence on Fg. FMPV/ODmax were related to thrombolytic treatment, the time of a disease.

### Conclusions

It indicated that hyperfibrinogenemia in plasma is one of pathologic basis of ACI, it was at peak at 24 hours and raised at 120 hours, continuous thrombotic treatment could make it reduced in UACI group, the wet weight and hypertension history were main effective factors on Fg. Abnormal FMPV was found to have notable influence on patients with TIA to be getting ACI, it was reduced at 12 and 120 hours, continuous thrombolytic treatment could reduce it from 12 to 120 hours, it indicated that FMPV is related to thrombolytic treatment or not at same time, systolic pressure and length of extrabody thrombus model. FMPV/ODmax was to be raised from 24 hours and it reached at peak at 168 hours, continuous thrombolytic treatment could prevent from its abnormal changes. BPC adhibit rate was at peak at 24 hours and thrombolytic therapy could make it reduce from attack 12 hours to 72 hours at the lowest level, but it began to be raised ones more. Our study showed that Fg and its molecular reactivity should be monitored in patients with ACI and thrombolytic therapy administered continuously. The anti-platelet aggregation drugs should be administered in order to prevent from cerebral infarction again. At same times, particularly in first 5 days increased dosage should be administered.

## Changes of Brainstem Auditory and Somatosensory Evoked Potentials in Late Infantile form of Metachromatic Leukodystrophy

OA

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### Objective

To investigate the characteristics and clinical value of evoked potentials in late infantile form of metachromatic leukodystrophy.

### Methods

Brainstem auditory and somatosensory evoked potentials were recorded in 6 patients, and compared with the results of CT scan.

### Results

All of the 6 patients had abnormal results of BAEP and MNSEP. The main abnormal parameters in BAEP were latency prolongation in wave I, inter-peak latency prolongation in I-III and I-IV. The abnormal features of MNSEP were low amplitude and absence of wave N9, inter-peak latency prolongation in N9-N13 and N13-N20, but no significant change of N20 amplitude. The results also revealed that abnormal changes in BAEP and MNSEP were earlier than that in CT.

### Conclusion

The detection of BAEP and MNSEP in late infantile form of metachromatic leukodystrophy might early reveal that abnormality of conductive function in nervous system and might be a useful method in diagnosis.

## The Effect of Nicotine on Bcl-2, Fas Protein Expression of Parkinson Mice

OA

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### Objective

Use MPTP to induce Parkinson disease model in C57 black mice, give acute intermittent nicotine, observe the behavioral changes, examine the subsequent effects of nicotine on the levels of Bcl-2 and Fas protein in substantia nigra neuron, probe into the possible protective mechanism of nicotine to neuron apoptosis.

### Methods

28 adult male C57 black mice were randomized divided into 4 groups: (1) normal control group; (2) nicotine group; (3) MPTP group; (4) nicotine plus MPTP group, 7 mice in each group. Give MPTP and/or nicotine for 5 days, observe the behavioral changes, perform pole and traction test. 24 hours after the last injection of drugs, take out whole brain, undergo continuous coronary section at the substantia nigra, use SABC method to carry out Bcl-2 and Fas immunohistochemical stain.

### Results

After MPTP injection, the mouse showed resting tremor, slowed movement accompanied by tremor, the scores of pole test and traction test was decreased obviously. The nicotine plus MPTP group was lightened than the MPTP group. The expression of Bcl-2 in MPTP group was decreased compared with control group ( $p<0.01$ ), increased in nicotine plus MPTP group compared with MPTP group ( $p<0.01$ ). The expression of Fas was increased in MPTP group compared with control group, decreased in nicotine plus MPTP group compared with MPTP group ( $p<0.01$ ).

## Conclusion

Nicotine can increase the Bcl-2 expression, anti the over expression of Fas gene caused by MPTP, thus can inhabit the substantia nigra neuron apoptosis, and have potential treatment value to Parkinson disease.

## Key words

Parkinson disease, MPTP, Nicotine, Bcl-2, Fas, Locomotor activity

## Poems Syndrome 538 Cases Clinical Analysis

OA

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## Objective

To investigate clinical characteristic and diagnostic regularity of POEMS syndrome.

## Method

Comparison of clinical data was made between 81 local patients (two patients seen in our hospital and 79 reported patients) and 457 patients from foreign countries.

## Results

The incidence rate of polyneuropathy, sexual hypofunction, hepatomegaly, lower extremities edema and skin pigmentation were similar between local and foreign patients. The incidence rate of myeloma, M-protein, diabetes mellitus, hypothyroidism and lymphadenopathy were lower in local patients. The incidence rate of dissociation between cell and protein of cerebrospinal fluid was higher in local patients. The cerebrospinal fluid protein was  $>0.4\text{g/l}$  in 75.6% of local patients.

## Conclusion

POEMS syndrome is a multi-system disease. Polyneuropathy and abnormal gammaglobulinemia are essential conditions to diagnosis POEMS syndrome.

## The Experiment Study on the Effect of Suo Yang About Learning and Memory and Effect of Ultrastructural in the Relevant Brain Areas of Learning and Memory in Rat's Model for Alzheimer's Disease

OA

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## Objective

The experiment studied on the effect of Suo Yang about learning and memory and effect of ultrastructural in the relevant brain areas of learning and memory in the rat's model of Alzheimer's disease.

## Method

Forty SD adult rats of 3 months age were trained for 3 days with maze galvanized and made them being familiar with maze line. Then 40 cases rats were divided into two groups: control group (C,10) was fed with distilled water; model group (M,30). The model group was further divided into three groups: model control group1 (10), model control group2 (10) and model treatment group (10). The time for the rat to pass the maze to the safe area was regarded as an index of the memory, sustaining excellent or inferior. M group rats were fed with  $\text{AlCl}_3$  liquor (50mg/100g/d) timely and continuously for two and a half months and made rats become the model of Alzheimer's disease. The change of synaptic ultrastructure was observed for all groups.

## Results

The time for passing the maze in the Model group was significantly extended  $P<0.01$ . The change was very marked in ultrastructure of

synapse relevant to the areas of learning and memory. The thickness of substance of the membrane of postsynapse was attenuated. After feeding Suo Yang for one month, the time taken to pass the maze in the MT group was reduced by about 39.74% and the thickness of substance of the membrane of the postsynapse was markedly thickened.

## Conclusion

The Chinese medicine Suo yang can markedly improved learning and memory of AZ model rats. This function is likely mediated through increasing the thickness of substance of the membrane of postsynapse relevant to brain areas.

## Key words

Suo yang, Rat, Alzheimer's Disease, Brain areas relevant to memory, Ultrastructure

## Asymptomatic Brain Stem Infarction of Senile Patients

OA

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In this article, 46 cases of senile patients with asymptomatic brain stem infarction were analyzed. Among which there were 35 men and other 11 were women, their average age were 67.58 years. CT was performed in 22 patients and MRI was performed in the other 24 patients. There were 38 cases of pons infarction, 2 cases of mesencephalon infarction and 6 cases of medulla oblongata infarction. The characteristics of the patients were that the brain stem infarction foci were found at CT scanning or MRI exam, and most of them were lacunar infarction which were the micro-infarction caused by the infarction of the deep branches of cerebral arteries. This kind of infarction had good prognosis which are very different from some severe brain stem infarction with high mortality. The majority of these patients come to hospital to consult for their symptoms and signs caused by the infarction of cerebral hemisphere and lobes, or for their transient cranial nerves injuries which were often ignored or explained with other reasons by patients or doctors. The reasons of brain stem infarction are same with those of other cerebral infarction. The diagnosis and treatment of the asymptomatic brain stem infarction are same as the routine method of cerebral infarction, the individual consideration is important. If possible MRI examination is necessary to confirm the diagnosis of the asymptomatic brain stem infarction.

## 帕金森病猴模型微囊化转TH基因细胞移植治疗实验研究

OA

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## 摘要

用海藻酸鈉/多聚賴氨酸(ALG/PLL)方法制造了包裹轉染有酪氨酸羥化酶基因(TH)的大鼠成肌細胞微囊。在體外,微囊內的細胞能長時間存活及生長,並能產生TH的蛋白。將這種微囊移植於正常猴的紋狀體,1個月後仍能在微囊內觀察到活細胞,而且移植處未見膠質細胞顯增生,在此基礎上,將這種微囊移植於患帕病(PD)的模型猴的紋狀體,初步觀察到其病理性能轉行為有明顯改善。

帕金森病(PD)是典型的神經退行性疾病,嚴重危害老年人的健康。它的病理特徵是中腦黑質多巴胺(DA)能神經元變性死亡,酪氨酸羥化酶(Tyrosine hydroxylase, TH)含量減少或活性下降,造成紋狀體內DA含量顯著降低而影響運動功能。藥物(左旋多巴)治療雖然有一定效果,但是長期用藥物後會產生難以耐受的副作用。移植腎上腺組織或胎腦也有一定療效,但是,其來源十分有限而且涉及倫理學等問題。

近年來,腦移植技術和基因轉移技術的結合,促進了PD基因治療研究,其中有種稱為ex vivo的方法,即在紋狀體內

移植轉基因的細胞，取得一些實驗結果。為避免宿主對移植細胞的免疫排斥，還發展了用聚合物包裹轉基因細胞，然後移植的新手段。本組以前的工作證明在PD大鼠腦內移植轉染有酪氨酸化疊基因(TH)的大鼠成肌細胞能取得明顯療效。本工作則試用海藻酸鈉/多聚賴氨酸包裹轉TH基因的大鼠成肌細胞，形成微囊的方法來克服異源細胞移植帶來的免疫排斥反應，在PD模型猴上探討該方法的可行性。

## Effect of Continuous Positive Airway Pressure Therapy in Patients with Sleep Apnoea Syndrome

OA

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### Objectives

To evaluate the efficacy and compliance of treatment for patient with obstructive sleep apnoea syndrome by continuous positive airway pressure (CPAP) therapy.

### Methods

A prospective study of 30 consecutive patients referred to Kwong Wah Hospital Electrodiagnostic Laboratory from March 1999 to May 2000 with newly diagnosed obstructive sleep apnoea commencing CPAP treatment were evaluated. Epworth sleepiness scale (ESS), objective CPAP compliance (hours of CPAP use per night), satisfaction with CPAP and side effects were assessed at 6 and 12 months.

### Results

There were 25 males and 5 females with mean ( $\pm$  SD) age of  $47.6 \pm 11.2$  years. The mean ( $\pm$  SD) ESS was  $13.0 \pm 4.9$  before the commencement of CPAP. There was a statistically significant decrease of ESS to  $5.9 \pm 3.6$  ( $p < 0.001$ ) &  $6.9 \pm 4.1$  ( $p < 0.001$ ) at 6 months and 12 months respectively. Objective CPAP compliance was  $5.1 \pm 1.1$  hours per night in average. 87% (20/23) of patients at 6 months and 95% (19/20) of patients at 12 months were satisfied with CPAP therapy and global improvement in general condition after commencement of CPAP.

The most common adverse events were dry mouth and nose (67%), nasal bleeding (54%), sore throat (33%) dizziness (21%) and headache (21%). Most treatment emergent adverse events were mild in severity. However, 7 patients discontinued the study at 6 months and 10 patients discontinued at 12 months. 72% of patients who discontinued CPAP therapy were unable to tolerate the CPAP machine, 24% of them stopped the therapy because of high machine renting cost and 18% of them were due to change of their working status.

### Conclusion

CPAP is an effective method for patients with obstructive sleep apnoea syndrome but tolerability for the machine remains a problem for long-term use.

## Ophthalmological Assessment of Visual Fields in Patients with Epilepsy

OA

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### Objective

Vigabatrin inhibits gamma-aminobutyric acid (GABA) transaminase and increase brain GABA levels. Experimental studies indicate that vigabatrin is neurotoxic and that the site of toxicity is proposed to be at the retina, where GABA is an important modulatory neurotransmitter. Recent reports have documented persistent visual field constriction, decreased b-wave in electro-retinogram and reduced Arden ratio in electro-oculogram in patients on long-term use of this medication. The

objective of this study to evaluate visual field changes, retinal nerve fibre layer (RNFL) thickness and to determine the prevalence of visual field (VF) dysfunction in Chinese patients on long-term vigabatrin treatment.

### Method

All patients with refractory seizures on vigabatrin for more than 6 months were assessed. Ophthalmological examination included visual acuity assessment, intraocular pressure measurement, complete slit lamp and fundal examination. Patients with glaucoma or family history of glaucoma were excluded. Visual field was evaluated by Humphrey full field 120-point standard screening test. RNFL values were measured using a Nerve Fibre Analyzer GDx. Ratio of superior to nasal quadrant RNFL thickness (S/N ratio) was measured.

### Results

32 eyes of 16 patients (10 females, 6 males, age range 9 to 36 years) were examined. Dosages of vigabatrin ranged from 500mg to 3000mg per day. All patients were asymptomatic with good visual acuity (range 20/20 to 20/40). No fundoscopic abnormalities were detected. Eight (50%) of the patients had evidence of visual field (VF) defects of which 93.8% were bilateral. 80% of the VF defects consisted of concentric peripheral field loss with central sparing. Superior/nasal ratio of RNFL thickness (S/N ratio) was significantly lower in those patients with VF defects:  $(1.5 \pm 0.37$  vs  $2.05 \pm 0.39$ ,  $p = 0.0034$ ).

### Discussion

The characteristics of VF changes are similar to those in Caucasian patients on long-term vigabatrin therapy. There was evidence of reduced RNFL thickness in cases with visual field defects; SN ratio was the best correlate. Retinal nerve fibre layer analysis may be another modality for monitoring the retinal toxic effect of drugs.

## The Expression of Growth Associated Protein-43 on Neuronal Plasticity of Ischemic Brain Stroke on Rats

OA

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### Objective

To investigate the changes of GAP-43 mRNA expression in the penumbra of cerebral infarction in spontaneously hypertensive rats and its relationship with clinical recovery of motor function.

### Method

The models of spontaneously hypertensive rat and middle cerebral artery occlusion (MCAO) were used. The fluorescence quantitative Rt-PCR associated with the in situ hybridization techniques were also employed to detect the level of GAP-43 mRNA expression in the brain tissue.

### Results

It was showed that, the GAP-43 mRNA expression was increased rapidly at day 3 following the MCAO. It reached the peak at day 7th and remained in a higher level than contrast until 14th day. This change was in inverse to neurological motor insufficiency score. The GAP-43 mRNA positive neurons mainly distributed in the penumbra of cerebral infarction and in the ipsilateral basal ganglia.

### Conclusion

There was a spontaneously process of neurite regeneration and functional recovery presented in the brain tissue of cerebral infarction in SHR. It was start-up as early as 3rd day and extended to the middle and late stage of cerebral infarction.

## Electrophysiological Findings in 12 Patients with Persistent Vegetative State in 24 Hour Dynamic EEG

OA

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### Introduction

The aim of this paper is to characterize, in detail, persistent vegetative state (PVS) patient in 24 hour dynamic EEG, and to verify if there exist an sleep-regulation in PVS. The recordings were evaluated for frequency, background activity, amplitude and sleep/wake cycle.

Subjects and methods: twelve PVS patient, 2 females and 10 males, participated to this study. All patients had MRI or CT scan materials, shown wide severe encephalatrophy. Their age ranged between 67 to 86 years (mean 72.34 years, SD 9.11) EEG performed in all of them. Signal were sampled 128 Hz and stored hard disk.

All recordings were 16 channel digital recordings using a Biologic Ceegraph SE digital machine. The electrode were placed according to the international 10/20 system, referenced to link earlobes (A1 and A2). Activation procedures included intermittent photic and sound stimulation. Hyperventilation was not performed due to the patients inability to comply with the procedure, EEG were recorded for a period of 24 hour.

### Result

1. Recordings shows diffuse slowing of background activity (diffuse polymorphous delta and theta activity)
2. All 12 of these who had low voltage, seven patients between 15 and 40 uv, and four patients lower 15uv
3. All of patients cannot be definite Alpha rhythm.
4. In 7 of 12 patients had not sleep / wake cycle.

### Conclusions

Wide severe cerebral cortex lesions lead to PVS, shown special conscious state and severe neurological deficits. In our studies, electrophysiological findings consist with MRI and CT. Diffuse Delta and Theta background activity, low voltage and no Alpha rhythm was the characteristics of our subjects. Most of the patients had not sleep/wake cycle.

## Cerebral Blood Flow Measured by the CVIQ Technique

SVIII

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Imaging investigations such as CT and MRI which have predominated in our clinical management of stroke only record the sequelae of the aetiological cause but cannot help in understanding how to prevent stroke occurring in any individual.

Treatment of stroke once it has caused cerebral infarction is unsatisfactory, and our prime aim must be to understand the diseases of the cerebrovascular circulation and abnormalities of perfusion these may cause.

Techniques that demonstrate the morphological state of the cerebral vessels (Angiography, DSA, CTA, MRA, Grey Scale Ultrasonography of the carotid arteries), do not reveal the haemodynamic disturbances that may result from any demonstrable abnormalities.

Techniques to study haemodynamics and perfusion are limited to certain restricted aspects of perfusion either flow velocities (Extracranial doppler, TCD) which are only one factor of actual flow volume, or relative distribution disturbances of perfusion (SPECT, PET, Xenon CT), and cerebrovascular reactivity (Xenon CT, PET).

Techniques that are clinically applicable to study true blood flow volume (BFV) have hardly been used in the study and management of stroke. These include Doppler flow volume, MRA Quantification, and Colour Velocity Imaging Quantification (CVIQ).

We have shown that of the three techniques CVIQ is probably the most accurate, closely followed by MRAQ. Doppler estimations are grossly inaccurate, because unlike CVIQ Doppler studies have been unable to allow for simultaneous temporal and spatial changes of flow, and vessel diameter.

We have been able to show the degree of BFV asymmetry in normal subjects, the BFV in the CCA, ICA, ECA, and VA, and total cerebral BFV, and relate this to the overall BFV in ischaemic states; estimation of reactivity; detection and quantification of collateral pathways in the presence of stenoses; the value of total cerebral BFV in prognosis of patients with stroke; and the effect of arrhythmias on total cerebral BFV.

CVIQ promises to reveal more interesting data on the nature of stroke and clinical applications in the future.

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