Joint Annual Scientific Meeting of the Hong Kong Epilepsy Society and The Hong Kong Neurological Society, 7-9 November 2003

Council of Hong Kong Epilepsy Society

Council of The Hong Kong Neurological Society

Guest Faculty

Scientific Programme

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Epilepsy Management: Matching Drugs to Patients

MJ Brodie

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Venue: Sheraton Hong Kong Hotel & Towers

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*N.B. Time for free paper / dissertation prizes presentation*
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Epilepsy Management: Matching Drugs to Patients

Martin J. Brodie
Epilepsy Unit
University of Glasgow
Glasgow, Scotland

The last 10 years have witnessed the global introduction into clinical practice of 9 new antiepileptic drugs (AEDs). These, together with the established agents, offer substantial choice to doctors treating patients with epilepsy. Most patients with recent onset seizures will be fully controlled with the first or second AED chosen often at moderate and even modest dosing. Since most patients diagnosed in adolescence or adulthood will require to take prophylactic AED therapy lifelong, it is important also to anticipate unacceptable side-effects and long term sequelae. The substantial choice of AEDs makes it possible to take a most holistic approach to epilepsy management. Consideration should be given to the patient’s seizures and/or epilepsy syndrome, age, gender, weight, co-morbidities, psychiatric history, concomitant medication and lifestyle when starting treatment. An alternative AED should be substituted if the first is ineffective or poorly tolerated. If two monotherapies fail or if the first AED produces a substantial improvement, a second drug with multiple mechanisms of action should be added. Attempts at seizure control should be made with two or three AEDs but never more. As more novel AEDs become available, the potential increasingly exists for synergism. A wide range of established and modern AEDs with different mechanisms of action, pharmacokinetics, spectra of efficacy, side-effects and interaction profiles are now available. We should make an effort to choose the best monotherapy and combination regimen for each individual patient. An aggressive approach to early optimization of seizure control may prevent the subsequent development of intractable epilepsy. Nevertheless, there is still a substantial minority of patients who are pharmacoresistant to the current AED armamentarium.

Free Paper Presentations

Re-exploring the Cerebrospinal Fluid (CSF) to Serum Glucose Ratio

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

Background
In interpretation of lumbar puncture (LP) findings, CSF glucose is conventionally expressed as a ratio to the simultaneous level in serum. A low ratio indicates hypoglycorrhachia and pathological conditions.

Method
We retrospectively studied the CSF findings in consecutive LPs performed in our ward over 5 years. Patients with conditions known to cause CSF hypoglycorrhachia, uncertain diagnosis and inadequate laboratory data were excluded. Blood for simultaneous serum glucose level was sampled within one hour of LP. ANOVA, Newman-Keuls multiple comparisons test and linear regression were used for statistical analysis.

Results
170 sets of samples from patients with central demyelination (45), neuropathies (66), headache (26), normal pressure hydrocephalus (11), neurodegenerative diseases (8), and others conditions (14) were studied. CSF glucose was <2.2 mmol/L in only one sample. Mean CSF to serum glucose ratio was 0.61 (range 0.21-1.00). Proportion of samples with ratios of <0.50, 0.50-0.59, 0.60-0.69 and 0.70 were 18.8, 27.1, 29.4 and 24.7% for all patients, and 6.8, 27.3, 38.6 and 27.3%, 60.0, 24.0, 8.0 and 8.0%, or 61.5, 30.8, 0.0 and 7.7% for patients with simultaneous serum glucose of <7.8, 7.8-11.1 or >11.1 mmol/L, respectively. Mean CSF to serum glucose ratios were significantly different between patients with simultaneous serum glucose of <7.8, 7.8-11.1 and >11.1 mmol/L (P <0.0001), but not for different neurological conditions (P = 0.5911). Linear regression showed a significant relation between serum and CSF glucose (r = 0.769, P <0.0001) and inverse correlation between serum glucose and CSF to serum glucose ratio (r = -0.569, P <0.0001, y = 0.8 - 0.03x).

Conclusions
Our study demonstrates the CSF to serum glucose ratio is not constantly related to but varies inversely with the simultaneous serum glucose level. A significant proportion of patients without conditions causing CSF hypoglycorrhachia has a low ratio during hyperglycaemia. The coefficient derived from our linear regression model can be applied for adjustment of such deviations.

Prestroke Cognitive Impairment in Stroke Associated with Small Vessel Disease

Prince of Wales Hospital, Shatin, Hong Kong

Objectives
Since in stroke associated with small vessel disease (SSVD), prestroke cognitive decline is associated with post stroke dementia, we studied the frequency, determinants, and outcome of prestroke cognitive impairment in SSVD.

Methods
Over a 6 months period, we administered Informant Questionnaire on Cognitive Decline (IQCODE) to close informants of 78 patients who were consecutively admitted to the acute stroke unit within 1 week of admission because of SSVD. Demographic data, vascular risk factors, apolipoprotein E, neuroimaging features (volume of white matter changes, number of silent small infarcts, cerebral atrophy index [CAI]), and outcome (stroke severity, cognition, Barthel index [BI], instrumental activities of daily living [IADL]) were compared between those with IQCODE >/= 3.4) and without (IQCODE < 3.4) prestroke cognitive impairment. Regression analysis was performed to find predictors of prestroke cognitive impairment.

Results
Nineteen patients (24.4%) had prestroke cognitive impairment. Multivariate regression revealed that only CAI (OR 1.48, CI 1.17 to 1.86, p<0.001) predicted prestroke cognitive impairment. Patients with prestroke cognitive impairment had greater impairment in cognition and IADL than those without it despite both groups having similar stroke severity and BI.

Conclusion
One quarter of patients with SSVD have prestroke cognitive impairment. Cerebral atrophy is associated with prestroke cognitive impairment. Those with prestroke cognitive impairment have more impaired post stroke cognition and IADL than those without it.

Hong Kong Childhood Stroke Registry (HKCSR) — A Study of 50 Cases (1991-2001)
B. Chung, V. C. N. Wong  
Department of Paediatrics & Adolescent Medicine,  
The University of Hong Kong, Hong Kong

Background  
A Hong Kong Childhood Stroke Registry (HKCSR) was established for Chinese children.

Objective  
To study the clinical presentation, etiology, risk factors and outcome of Chinese children with stroke.

Materials and Methods  
A prospective childhood stroke database was collected during 1991-2001 for children with stroke seen in the University of Hong Kong. Neonatal strokes were excluded.

Results  
Fifty children (boys: girls = 28: 22) with mean age of 5.4 years were included. The commonest presenting features were seizures and hemiplegia. There were 36 ischemic and 14 haemorrhagic strokes. For ischemic stroke (36), 18 were due to thrombosis - 11 were vascular origin [moya-moya disease (3), neurofibromatosis (2), fibromuscular dysplasia (1) and post-infectious vasculitis (7)]; 5 were haematological [leukaemia (3); thalassaemia (2)]; and 1 each with severe dehydration and Mitochondrial Encephalopathy Lactic Acidosis Syndrome. Of 15 cases with embolic stroke, all had underlying congenital heart diseases. For 14 cases with haemorrhagic stroke, 2 had arteriovenous malformation, 7 had bleeding tendency [leukaemia (2), aplastic anaemia (2), hemophilia (2) and Wiskott Aldrich Syndrome (1)] and 2 had >1 risk factors [leukaemia and sepsis; congenital heart disease with streptokinase infusion after cardiac catheterization]. Six (12%) were idiopathic. None had sinusovenous thrombosis.

Outcome  
The mean follow-up was 6.6 years (1.8-12.4 years). Nine (18%) died, with 5 having ischemic stroke and 4 with hemorrhagic stroke. 44% had neurological deficit, including mental retardation (11), epilepsy (9) and hemiplegia (14). Five had recurrent stroke. Decreased consciousness (p=0.004), hematological cause (p=0.04) and hemorrhagic transformation of ischemic stroke (p=0.01) were associated with high mortality. Of the 41 survived, the only significant risk factor for long-term neurological deficit was seizure at initial presentation (p=0.04).

Conclusion  
The incidence of childhood stroke from our series is 1.7 per 100,000 children per year. The majority had thrombo-embolic stroke. The majority who survived had neurological sequelae.

Outcome of Children with First Febrile Seizure — A Local Cohort Study of 565 Cases  
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Objective  
To investigate the clinical profile and outcome of children admitted for first febrile seizure (FS) in Hong Kong.

Methods  
A retrospective study was performed for all children admitted to Queen Mary Hospital with first episode of FS for during a 5 years period (March 1998 - March 2003) was conducted. FS is defined as "an event in a neurologically healthy infant or child aged 6 months to 5 years, associated with fever >38°C but without evidence of intracranial infection or a defined cause and with no history of prior afebrile convolution" (1). Children with pre-existing developmental delay or underlying neurological disorders were excluded.

Results  
Of 1113 children admitted during this period with ICD-9 coding of 780.31 for FS, only 565 children were admitted for the first FS. This First FS database consisted of 565 children (boys: girls = 1:4:1). The mean age of onset was 2.1 +/- 1.1 years. Eighty four percent (474/565) was simple FS and 16% (91/565) was complex FS. Family history of FS and afebrile seizures were present in 17.5% and 2.7% respectively.

Conclusion  
The commonest infection is upper respiratory tract infection (75%), followed by gastroenteritis (6.3%), lower respiratory tract infection (4.8%), rosea infantum (3.4%), urinary tract infection (1.4%) and clinical sepsis (1%). The isolated organisms included influenza A (11.8%), adenoavirus (4.8%), parainfluenzae (4.3%), Respiratory Syncytial Virus (2.7%), influenza B (2.1%) [all from nasopharyngeal aspirate], Rotavirus (1.4%) and salmonella (1.4%) [from stool]. There was no significant difference between age of onset, sex, family history of FS, types of infection or causative organisms with presentation as simple or complex FS.

The mean follow-up period was 2.33 +/- 1.69 years. Altogether 103 children had recurrence of FS - with 72% (74/103) having 1 recurrence, 17.5% (18/103) with 2 and 10.5% (11/103) with more than 2 recurrences. The overall recurrence rate was 12.7% by 1 year, 18.7% by 2 years and 20.5% by 3 years.

Early age of onset [p=0.04; OR = 1.9 (95% C.I. = 1.23-2.95)], family history of FS [p=0.04; OR = 1.8 (95% C.I. = 1.07-3.09)] and complex FS [p=0.005; OR = 1.85 (95% C.I. = 1.02-3.27)] were statistically significant risk factors for recurrence. Only 2 children (0.4%) developed afebrile convulsion during follow-up.

Conclusion  
The estimated incidence of first FS in our local children is 0.3%. The overall recurrence rate for FS was 20%. Risk factors of recurrence were similar when compared with Caucasians. Type of infections and causative organisms were not important determining factors for recurrence from our study.

Reference  

Selective Doral Rhizotomy in Children with Spastic Cerebral Palsy  
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Background  
Spasticity in children with cerebral palsy has many adverse effects on patient’s normal daily function. Selective dorsal rhizotomy (SDR) is one of the many effective surgical options in managing spasticity. SDR has been performed in Tuen Mun Hospital since 1996. Modifications on patient selection and surgical technique continue to be revised every year. We present our latest 2-year experience in managing spastic cerebral palsy children with SDR.

Method  
11 patients have undergone SDR between the period of August 2001 to August 2003. The extend of dorsal root to be excised were then compared.

Hong Kong Med J Vol 9 No 6 December 2003 Supplement 2 9
Epilepsy Surgery for Refractory Temporal Lobe Epilepsy: Review of 32 Cases

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Background
About one third of epilepsy patients attending the neurology clinic in public hospital in Hong Kong have intractable seizures. Among the different epileptic syndrome, temporal lobe epilepsy was the commonest clinical entity. There is limited information on efficacy of epilepsy surgery in Chinese. We studied the results of consecutive patients known to have intractable temporal lobe epilepsy and underwent surgical resection in two regional hospitals in Hong Kong.

Objective and Method
Patients with refractory TLE despite adequate and appropriate medical treatment were eligible for the epilepsy programme. Patients with systemic illness like renal or liver failure, co-existing moderate to severe mental retardation or acute psychiatric illness were excluded. They underwent clinical, electroencephalographic and laboratory parameters of the disease. Pathological substrates include 21 cases of mesial temporal sclerosis, 6 neoplastic lesions, 4 vascular lesions and 1 cystic lesion. The patients and Methods

Results
32 patients were operated from 1996 to 2002: 10 male and 22 female cases, mean age 31 years (range: 14-48). Pathological substrates include 21 cases of mesial temporal sclerosis, 6 neoplastic lesions, 4 vascular lesions and 1 cystic lesion. The duration of seizure before surgery ranged from 11 to 40 years. The patients was studied prospectively and consecutively by clinical examination, laboratory test and neurophysiological studies.

Conclusion
The results of epilepsy surgery in this group of Chinese patients are consistent with overseas series. However, in view of relatively long seizure period prior surgery and small proportion of patients being benefited, expansion of the program was necessary for better management of this group of pharmaco-resistant epilepsy.

Myasthenia gravis (MG) is undoubtedly the most thoroughly understood of all autoimmune diseases and has served as a model for the elucidation of mechanisms underlying other autoimmune disorders. It is caused by antibodies directed against acetylcholine receptors at the neuromuscular junctions. Most patients are now effectively treated with cholinesterase inhibitors, immunosuppressive agents or thymectomy. Our knowledge of MG has changed dramatically over the past four decades. As our understanding of the disease has improved, the diagnostic and treatment strategies have also changed. More patients were being identified at the earlier stage of the disease.

This is a retrospective cohort study of patients with myasthenia gravis (MG) who have received treatment at a tertiary care hospital in Hong Kong. A total of 185 patients (90 males, 95 females) were included. Hypothyroidism, the most commonly associated autoimmune disease, was present in 17.3% of patients. Moreover, 25% of patients initially presented as ocular symptoms developed into generalized MG later, and the average duration of generalization was 43 months. CT thorax had a high yield in detecting thymoma in MG patients (with specificity of 92% and positive predictive value of 81%). In comparing the groups of generalized patients with or without acetylcholine receptor antibodies (AChR-Ab), the incidence of thymoma in seropositive patients was significantly higher than the seronegative patients (35.7% versus 2.9%). Also the predominance of "ocular bulbular" presentation was absent in seronegative patients, and no difference was noted in the rate of complete remission between the two groups. Most patients with resection of thymoma had favorable outcomes, but 6 of the 27 patients had tumor recurrence. Anti-striated muscle antibodies were more common in patients with thymoma than those without thymoma (84.2% versus 15.4%). In non-thymoma generalized patients, thymectomy also offered a better outcome than those without thymectomy. 64.9% of patients achieved symptom-free status after receiving various treatment modalities. Altogether 11.9% of patients experienced myasthenic crisis at any time of their course of disease. With the advances in critical care and mechanical ventilation, no mortality was observed in patients with myasthenic crisis.
be present in 34.2% of the patients. Half of them (55.3%) had positive neuropathy symptom score but more than 70% were found to be normal on neurological examination. The most frequently affected nerves were, in descending orders, sural nerve, superficial nerve, median nerve, common peroneal nerve and posterior tibial nerve. Advance age, positive of anti-RNP antibody and use of azathioprine were the parameters found to be significantly associated with the development of peripheral neuropathy.

Conclusion
The prevalence of neurological manifestations are relatively high among Chinese SLE patients. Low complement level, presence of anticardiolipid antibody and use of cyclophosphamide were risk factors for development of neurological manifestations. The considerable frequency of subclinical peripheral neuropathy and absence of associated clinical parameter makes it necessary to carry out neurophysiological studies in these patients to detect its presence and establish the precise extent of the disorder.

SYMPOSIUM II — PFIZER SYMPOSIUM ON STROKE

IMT, Hypertension and Stroke

Pierre-jean David Toublou
(no abstract available)

Hypertension and Vascular Lesions in Chinese
Lawrence Wong
(no abstract available)

SYMPOSIUM III — SYMPOSIUM ON NEUROLOGY

UPDATE

Management of Vascular Dementia

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Interest in the management of vascular dementia (VD) has increased over the last decade. VD is the second most common cause of dementia. It encompasses 2 major subgroups—subcortical vascular dementia (SVD) associated with small vessel disease and cortical vascular dementia associated with multiple atherothrombotic or embolic strokes. Recent clinical trials have demonstrated the efficacy of 2 acetylcholinesterase inhibitors (AChE I), donepezil and galantamine, in improving cognition of patients with VD. Post-hoc analysis also revealed that donepezil was effective in patients with either cortical or subcortical VD. Rivastigmine is another AChE I that also possess anti-butyrylcholinesterase action. A pilot study is underway in evaluating the safety and efficacy of rivastigmine in Chinese patients with SVD. Other non-cholinergic agents that have been shown to be effective in small clinical trials include memantine, nimodipine, and pentoxifylline.

Prevention of VD has also been a major research focus in recent years. Results of the Syst-EUR trial suggested that treatment of 1000 elderly patients having systolic hypertension with nitrendipine for 5 years could prevent 20 cases of dementia. In PROGRESS, perindopril based therapy was found to decrease the incidence of stroke related dementia by 34%. A recent prospective observational study has found that participation in cognitive activities is associated with reduced risk of VD. In a recent post-hoc analysis, simvastatin was found to retard progression of cerebral white matter changes among Chinese patients with severe white matter changes.

Furthermore, elevated levels of LDL cholesterol were found to associate with risk of stroke related dementia in elderly Caucasians. Clinical trials are needed to explore the effect of lipid lowering agent and participation in cognitive activities in the prevention of VD.

Neuropathic Pain Management

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Neuropathic pain is defined as pain initiated or caused by a primary lesion or dysfunction in the nervous system. Examples of this condition include post-herpetic neuralgia, trigeminal neuralgia, diabetic neuropathy, complex regional pain syndromes, phantom limb pain, scar pain, post-incisional pain etc.

Neuropathic pain causes physical and psychological debility resulting in considerable suffering and disability. The management of neuropathic pain conditions remains a considerable challenge despite major advances. The pathophysiology is complex and involving many postulated mechanisms in the central and peripheral nervous system.

The patient with chronic neuropathic pain usually presents as a complex of pain conditions with possibly protein and confusing presentations. Apart from neuropathic pain, patients usually have other secondary conditions e.g. muscular-skeletal pain which can give rise to a confusing array of presentations. Consequently diagnosis can be challenging and late diagnosis is not uncommon.

The diagnosis is based on history and physical examination. The condition usually presents with allodynia, hyperalgiesia, hyperpathia, abnormal spontaneous pain, paresthesia and dysaesthesia. Laboratory tests, electrophysiological tests and imaging examinations may not be necessary as the absence of positive findings does not exclude diagnosis of neuropathic pain.

Definitive treatment remains elusive. Treatment involves many approaches with medications as the mainstay of therapy. Recently, new approaches and medications have been used. However, treatment remains difficult. Early diagnosis and aggressive interventions are critical to improve chances for a better outcome.

SYMPOSIUM IV — UCB SYMPOSIUM ON EPILEPSY

New Development of Treatment for Epilepsy

Bo Leppik
(no abstract available)

Pathogenesis of Refractory Epilepsy: Focus on the Drug Transporter P-glycoprotein

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The pathogenesis of pharmacoresistance in epilepsy is unclear. One of the candidate mechanisms for drug-resistant epilepsy that has attracted growing interest recently is limitation of drug access to the seizure focus in the brain by the drug transporter P-glycoprotein (P-gp), encoded by the multi-drug resistance (MDR1 or ABCB1) gene in man. It is predominantly expressed in organs with excretory functions (e.g. liver, kidney, gastrointestinal tract) and at blood-tissue barriers, e.g. testis, placenta. The high level of P-gp in the cerebrovascular endothelium is believed to contribute to the functionality of the blood-brain barrier. P-gp mediated efflux
is thought to act as a physiological defence mechanism, extruding xenobiotics from mammalian cells and affording protection of sensitive organs.

There is mounting evidence to support the hypothesis that overexpression of P-gp in the cerebrovascular endothelium, in the region of the epileptic focus, may limit the access of antiepileptic drugs to their site of action and thus play a causative role in refractory epilepsy. This hypothesis is supported by the findings of elevated MDR1 expression in epileptic foci in the brain of patients with drug-resistant epilepsy, induction of P-gp expression by seizures in animal models, and experimental evidence that some commonly used AEDs are substrates for P-gp mediated efflux.

MDR1 expression has been found to be controlled by a relatively common single nucleotide polymorphism, C3435T in exon 26. Further studies suggest that there is considerable ethnic variation in the frequency of the C3435T genotype. Results from a recent association study among Caucasian epilepsy patients suggest that the C/C genotype may be associated with medical intractability. Further studies to delineate the exact role of MDR1 gene expression in drug resistant epilepsy from cellular to population genetics levels, and to devise methods to circumvent its effect, are warranted.

### A Population Based Epidemiological Study of Epilepsy in Hong Kong

G. C. Y. Fong, P. Kwan, A. Hui, C. Lui, J. K. Y. Fong, V. Wong

**Background**

Epilepsy is a common neurological disorder. Epidemiological data is crucial for physicians and health care administrators in managing patients with chronic diseases like epilepsy. Prevalence and incidence of epilepsy have been found to vary among countries with different geographical and cultural backgrounds. Compared to a community based study conducted in a Chinese population showing a prevalence of 4.4 per 1000, previous local center-based surveys in Hong Kong suggested a prevalence of 0.45 to 1.54 per 1000. In this communication, we reported the first population-based epidemiological study of patients with seizure disorders in the Hong Kong Special Administrative Region (HKSAR) of China.

**Methods**

The study is being conducted in two stages: a telephone-screening phase followed by clinical validation. The telephone interview was conducted between July and August of 2003 by the Social Science Research Center of The University of Hong Kong, using a validated questionnaire, with 7 questions, modified from the WHO neuroscience research protocol. 9547 fixed-line telephone numbers were randomly selected and adults older than 15 years were invited for this survey. Every household member, of any age, was assessed during the telephone interview. For practical reasons, households more than 5 members was truncated and the elderly 5 members were evaluated by the questionnaire. 5178 (54.2%) households completed the questionnaire successfully, covering a total of 17783 persons. (Estimated sampling error ± 0.75%). The demographic data of the respondents completed the telephone interview is similar to that of the general population of Hong Kong reported in the 2001 census. Positive respondents would be invited for clinical validation by board-accredited neurologists.

**Results**

Episodes of loss of consciousness were reported by 357 (2.0%) subjects, features compatible with generalised tonic clonic convulsion by 199 (1.1%), drop attacks or urinary incontinence or tongue biting by 174 (1.0%) features compatible with complex partial seizures by 109 (0.6%) febrile convulsion by 254 (1.4%), and 48 (0.3%) subjects have been told to have epilepsy or seizure disorders by their physicians. Overall, 685 (3.85%) subjects gave positive response to one or more of the above questions. 504 (2.8%) subjects had undergone electroencephalographic examination in their lifetime. 232 households with positive responses were agreed to be contacted for clinical validation. Positive respondents were invited for clinical validation by board-accredited neurologists.

**Conclusion**

Epilepsy is a common disorder and it appears to be more common among the general population in Hong Kong than previously thought. Clinical validation is underway to confirm the diagnosis and sub-classify the seizure disorders among the positive respondents.
EPILEPSY SURGERY I

Evaluation and Surgical Management of Refractory Epilepsies

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Despite recent progresses in medical management of epilepsies, approximately 30% of patients do not respond to adequate drug therapy. Those patients having drug resistant epilepsies (DRE) comprises the major burden of epilepsy care and often carries a high risk of psychosocial handicap, poor quality of life, and SUDEP. Epilepsy surgery is certainly a vital therapeutic alternative for patients suffering from DRE. Modern concept of epilepsy surgery was initiated by Dr. Horsely in 1886, rapidly developed by application of EEG and its related technologies, and then widely spread to epilepsy communities by virtue of progresses in neuroimaging. Recently, Wiebe et al (2001) conducted a randomized clinical trial of surgery in refractory temporal lobe epilepsies and clearly proved its superior efficacy over the continuing drug therapy. Therefore, surgical therapy in patients suffering from refractory temporal lobe epilepsies and also probably in various surgically remediable epilepsies syndromes in (SRES) should be regarded as an essential therapeutic modality rather than an option. On the other hand, patients with DRE not belonging to SRES may still require a prolonged systematic drug trials before considering surgery.

The presurgical evaluation consists of various procedures including video-EEG monitoring (non invasive or invasive), neuroimaging, and neuropsychological evaluations. All these tests are conducted to accurately determine the extent of epileptogenic zone and the extent of surgical resection without causing unacceptable neurological deficits. The best predictor of successful surgical outcome is not the evidence from any one single test but the concordant results of various tests. It should be emphasized that the individuals requiring surgery have quite heterogeneous conditions and the success of surgery cannot be guaranteed in any patients. The data obtained from a battery of tests performed in each patient should be thoroughly analyzed and carefully synthesized in a team conference to achieve the optimal outcome.

Diagnostic Neuroimaging for Epilepsy

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There is little question that recent advances in neuroimaging particularly Magnetic Resonance imaging (MRI) have revolutionized the evaluation and treatment of epilepsy and seizure disorder. Epilepsy usually requires long-term pharmacotherapy or, in selected cases, neurosurgical intervention. Neurosurgery is most often considered in medically refractory epilepsy when removal or isolation of the epileptogenic region is possible without unacceptable neurologic deficit. Pre-operative assessment including localization and lateralization of the epileptogenic region and delineation of eloquent area are important. Our center combines scalp EEG and Neuroimaging including MRI and SPECT scan, in addition to clinical semiology, for epilepsy investigation. If the results are discordant, operation is planned with the knowledge of eloquent area from functional Neuroimaging such as fMRI and WADA test. In cases with discordant EEG and Neuroimaging findings or when confirmation of the epileptogenicity of the MR-identified lesion is lacking, intracranial EEG recordings using subdural strip or grid are warranted.

The primary role of MR is to locate and characterize the structural abnormality responsible for epileptogenesis. The MR sensitivity varies for different epileptogenic lesion (substrate). Tumour: 100%, Neuronal Migration disorder: 90-100%, Vascular Malformation: 100%, MTS: 90-95% and Neocortical sclerosis: 80-90% (Jack C et al). The other roles of MR in epilepsy include pre-operative assessment (determine the eloquent area) and post-operative follow-up. New MR technique using 3D volumetric Spoiled Gradient Echo imaging with surface rendering reconstruction could increase MR sensitivity. The advanced MR Imaging such as MR spectroscopy (MRS) and functional MRI (fMRI) will assume an increasingly role in epilepsy surgery. Physiologic Imaging includes SPECT and PET scans have been used for localization of the epileptogenic zone. The interictal PET and SPECT demonstrate a zone of hypometabolism and hypoperfusion respectively. However, an interictal SPECT study alone is not reliable. Correlation with ictal SPECT scan (showing hyperperfusion) or MRI is essential. Ictal SPECT scan achieved 97% correct localization of lesion as compared with 71% for postictal SPECT and 48% for interictal SPECT scan. WADA test is sometimes performed before the operation. The Neuroimaging (anatomic and physiologic) has increasing important role in epilepsy management.

Memory Deficits After Resection from Anterior Temporal Lobe

Tatia Lee

(no abstract available)

EPILEPSY SURGERY II

Surgical Treatment for Mesial Temporal Lobe Epilepsy

Joseph Lam, Andrew Hui, Patrick Kwan, Y. L. Chan, M. C. Cheung, Agnes Chan, P. W. Ng, W. S. Poon

Literature Review

Temporal lobe epilepsy (TLE) is a well-defined focal epilepsy syndrome. Based on the location of the epileptogenic zone and the pathological etiology, TLE can be further divided into mesial and neocortical TLE. The epileptogenic zone for Mesial Temporal Lobe Epilepsy (MTLE) is from the hippocampal formation or the amygdala. The most common pathological etiology for MTLE is mesial temporal sclerosis (MTS). A high percentage of MTLE is refractory to medical treatment. Moreover, seizure frequency and severity tends to increase with time.

The two main forms of surgical treatment for MTLE are Anterior Medial Temporal Resection (AMTR) and Selective Amygdalohippocampectomy. The aim of both operations was to remove diseased hippocampal formation and amygdala. Comparative studies showed there is no significant different in post-operative seizure outcome. The seizure-free outcome 1 year after hippocampal resection varies between 67% to 80%. The seizure free outcome dropped to around 62% at 5 years. (Berkovic 1995) AMTR consists of anterior temporal lobectomy and amygdalohippocampectomy. Both standard 3 cm resection of the anterior hippocampus and radical resection up to the tail at the posterior margin of the midbrain were described with similar seizure control rate. Whether one should take the addition risk of performing radical excision is not clear.

Studies suggested that irrigating the hippocampus using gamma knife can be effective for seizure control. (Regis 1999) Experience with gamma knife is less than that with surgical resection. Vagal nerve stimulator (VNS) may be an alternative for patients with MTLE but not suitable for hippocampal resection after work-up. Seizure control with VNS is less effective then surgical resection.
Preoperative work up may include, EEG, video EEG, PET scan, ictal SPECT, MRI scan, functional MRI scan, neuropsychological tests and WADA test. The primary aim is to ensure that the target hippocampus has abnormal function and is the epileptogenic focus. The secondary aim is to decide if the remaining hippocampus can support the memory function of the patient after resection of hippocampus on one side.

Failure of seizure control after hippocampal resection may be related to presence of bilateral epileptogenic hippocampal pathology, and/or extrahippocampal neocortical lesion (such as microscopic cortical dysplasia). Accurate preoperative case selection and adequate surgical resection are the two factors that may be improved for better seizure control.

Local Experience
The standard preoperative assessments in our epilepsy surgery programme include, EEG, video EEG, MRI scan, functional MRI scan, neuropsychological tests and WADA test. Our study using functional MRI for language function localization showed that in the local population, the Broca’s area is usually activated when reading English, however, the premotor frontal area are more commonly activated when reading Chinese. The language area is seldom located in the region to be resected.

We reviewed our cases with AMTR performed since 1998 with minimum FU of 1 year and a median FU of 3 years. We compared the seizure control rate between the standard resection (4 cases) and radical resection (9 cases). The seizure control on each year of follow-up was classified according to the International League Against Epilepsy (ILAE) classification. The Engel Classification was used for the final grading.

Results
Overall, 69% (9/13) were seizure free (ILAE class 1 or 2) at 1 year and 63% (5/8) at 3 years. All the cases showed improvement in seizure control. The final Engel classification was 54% (7/13) in Class I, 15% (2/13) in Class II and 31% (4/13) in Class III. None suffered from serious or disabling complications. All the patients can continue their preoperative occupation.

For the radical resection, the seizure free % maintained well over time: 67% (6/9) at 1 year and 75% (3/4) at 3 year. For the standard resection, seizure free % drop from 75% (3/4) at 1 year to 50% (2/4) at 3 years. The initial seizure control was similar between standard and radical resection, but with longer FU the radical excision group showed longer lasting seizure control than the standard resection group.

Conclusion
AMTR is a safe and effective treatment for control of medically refractory MTLE based on external and local experiences.

References
**Microvascular Decompression for Refractory Trigeminal Neuralgia**

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**Background**

Trigeminal neuralgia (TN) is a common microvascular compression syndrome of cranial nerves. Medical treatment is regarded as the first line treatment; however, a group of patients do not respond to medical treatment satisfactorily and develop persistent and refractory symptom(s). Surgical microvascular decompression (MVD) is usually then advised. We reviewed the surgical MVD outcome of this group of patients.

**Methods**

From year 1998 to 2002, patients, underwent MVD for trigeminal neuralgia refractory to medication, were reviewed. Symptomatology, duration of symptoms, drugs use and surgical outcome were reviewed.

**Results**

Total of 14 patients underwent MVD for refractory TN between 1998 and 2002. The median age of patients was 61 years (25-76). The median duration of symptom was 4.5 years (1-16). Preoperative MRI scan detected relevant abnormality in 8 cases with 6 vascular loops and 2 tumors. Symptom control was unsatisfactory despite multiple medications (average-3). Complete symptom relief was achieved in 71% (10/14) of the patients. Three patients had partial symptom relief (>50% relief in pain score). Symptom relief was observed early after surgery with 93% immediate improvement and 7% improvement within the first week. The median follow-up time was 2 years and 9 months and no recurrence of symptoms was recorded. Transient facial paresthesia was observed in 2 patients and 1 patient developed a subclinical cerebellar hemorrhage.

**Conclusion**

Microvascular decompression (MVD) is an effective and safe treatment for patients with trigeminal neuralgia refractory to medications. All of our patients responded to surgery with 71% of complete symptom relief. MRI scan is not sensitive in detecting vascular culprit but it is essential to rule out other compressive causes.

**The Effects of Disease Severity, Use of Corticosteroids and Social Factors on Neuropsychiatric Complaints in Severe Acute Respiratory Syndrome (SARS) Patients at Acute and Convalescent Phases**

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**Background**

Princess Margaret Hospital held the largest cohort of Severe Acute Respiratory Syndrome (SARS) during the outbreak. We performed a questionnaire survey to evaluate the neuropsychiatric complaints in SARS patients at acute and convalescent phases and their associations to the disease severity, use of corticosteroids and social factors.

**Methods**

Four sets of identical self-administered questionnaires, designed to assess the various neuropsychiatric domains, were mailed to 308 SARS survivors and their families. Both patients and families were asked to complete two questionnaires for the neuropsychiatric symptoms in acute and convalescent phases respectively. We used factor analysis to explore the construct of the symptoms and calculated the factor scores for each construct. Constructs identified from the factor analysis were used as dependent variables in the multiple linear regression model to study the relative contributions from disease severity, corticosteroids and social factors.

**Results**

Among the 102 (33%) replies, 65% had strong symptoms that would require psychiatric consultation. Dosage of pulse steroid and accumulated dosage of corticosteroids used in acute phase were predictive for anxiety-depression, psychosis and behavioural symptoms during acute phase. They were also predictive for anxiety-depression and worse psychological well-being at convalescent phase. Disease severity had direct correlation with symptoms in all neuropsychiatric domains at acute phase and anxiety-depression, psychological well-being and manic symptoms at convalescent phase. Health care workers had more neuropsychiatric complaints in both phases. Severity of symptoms, corticosteroids and social factors explained about half of the variances (R²=52) in anxiety-depression at acute phase and 33% at convalescent phase.

**Conclusions**

Disease severity, use of corticosteroids and being health care workers were independent predictors of neuropsychiatric complaints in both acute and convalescent phases.

**Comparing Seizure Control Rate Between Standard and Radical Amygdalohippocampectomy**

J. M. K. Lam, A. C. F. Hui, P. Kwan, Y. L. Chan, A. Chan, P. W. Ng, W. S. Poon

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**Background**

The anterior medial temporal resection (AMTR) is the standard procedure for medial temporal lobe epilepsy (MTLE). AMTR consists of anterior temporal lobectomy and amygdalohippocampectomy. Both standard 3 cm resection of the anterior hippocampus and radical resection up to the tail at the posterior margin of the midbrain were described with similar seizure control rate. Whether one should take the addition risk of performing radical excision is not clear.

**Material & Methods**

We reviewed our cases with AMTR performed since 1998 with minimum FU of 1 year and a median FU of 3 years. We compared the seizure control rate between the standard resection (4 cases) and radical resection (9 cases). The seizure control on each year of follow-up was classified according to the Internal League Against Epilepsy (ILAE) classification. The Engel Classification was also used for the final grading.

**Results**

Overall, 69% (9/13) were seizure free (ILAE class 1 or 2) at 1 year and 63% (5/8) at 3 years. All the cases showed improvement in seizure control. The final Engel classification was 54% (7/13) in
Mitochondrial encephalomyopathies, MELAS is the only type with stroke and seizures as prominent features. The proportion of mutant to normal mtDNA varies among different tissues and is termed heteroplasmy.

Methods
We recorded the clinical, laboratory, histopathological, imaging and genetic analysis results of consecutive patients presenting with MELAS syndrome from a regional hospital.

Results
Four unrelated patients, three female and one male, were reviewed, all presenting before 40 years of age. Presenting features were seizures and acute stroke (two patients each). A history of spontaneous abortion, normal early development, diabetes mellitus, recurrent headache and vomiting were common. Clinical features included short stature, generalized tonic-clonic convulsions, retinitis pigmentosa, sensorineural deafness, dysarthria, dysphasia, hemiparesis, homonymous hemianopia and Wolf-Parkinson-White Syndrome. There was a history of premature deaths in two siblings of affected patients. Investigations revealed ragged-red fibres in striated muscle on muscle biopsy, computed tomography and brain magnetic resonance (MR) imaging evidence of cortical and subcortical white matter infarcts and MR spectroscopy demonstrating increased lactate in infarct free areas. One patient died following status epilepticus. Genetic analyses on three of the patients revealed base pair substitution of tRNA at 3243.

Conclusions
Phenotypic variability is common in these disorders; the diagnosis of MELAS should be considered particularly in young patients presenting with strokes or in association with epilepsy.

Hospital Arrival Time After Acute Stroke
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Methods
We undertook a survey of secular trend of acute ischaemic stroke presentation time and compared the results to a similar study conducted over 10 years ago, using the same methods and survey instruments within the same hospital.

Results
In the 1989 study, 501 patients (mean age 70 ± 12 years) were admitted with acute ischaemic stroke; 29% of patients arrived at the hospital within 4 hours, 45% of patients within 8 hours. During a four-month period in 2002, among 321 cases (mean age 71 ± 11 years), 36% had an arrival time less than 4 hours. Median presentation time was 9 hours after stroke onset.

Conclusion
This observational study showed a temporal trend of improving...
hospital arrival times after acute ischaemic stroke. Reasons for this may include greater public awareness, improvement in pre-admission ambulance service or a smaller catchment area as compared with 1989.

Influence of Emergency Room Fee on Acute Stroke

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Background
With the recent introduction of emergency room fees at public hospitals patients seeking medical care are required to pay a basic charge. We hypothesize that this would discourage patients from seeking prompt medical advice. This observational study sought to evaluate timing of patient presentation with acute stroke and to evaluate whether there is difference in presentation delay before and after the introduction of emergency consultation fee system.

Methods
All consecutive patients presenting with acute stroke and admitted to the medical wards of our hospital over two specified two-month periods before and after the new fee system were enrolled. Cases were ascertained from the computerized admission and discharge records of the emergency and the medical department. We recorded the onset of neurological symptoms prior to presentation to the emergency department and the interval, in hours, between the onset of stroke and arrival time at the emergency department. We tested for associations between presentation interval before and after the new system.

Results
A total of 173 subjects were recruited before, and 189 after, the introduction of consultation fee system. The median time for presentation was 9.7 hours and 8.4 hours respectively (p = 0.66). Acute ischemic stroke accounted for 91% of the stroke diagnosis, mean age of patients was 71 years. Unconsciousness upon arrival at emergency department was more likely to be associated with a presentation interval of less than 5 hours (odds ratio 0.18, CI 95% 0.08-0.42, p < 0.0001). Age was significantly associated with presentation delay (r = -0.14, p = 0.08). A higher proportion of stroke patients admitted after the consultation fee system, on the other hand, were unconscious upon arrival (12% versus 6%, p = 0.04).

Conclusion
We did not demonstrate a delay in acute stroke presentation with the emergency room fee system. However physicians should continue to explore strategies for reducing late presentation of acute stroke.

Effects of Electrical Stimulation of Vagus Nerve for Treatment of Refractory Epilepsy

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Background
Vagal nerve stimulation (VNS) is an adjunctive treatment for patients with refractory partial-onset seizures. We conducted a prospective, observational trial on the long-term efficacy and safety of VNS in Chinese patients.

Methods
Adult patients with clinical evidence of chronic pharmacoresistant epilepsy underwent pre-surgical evaluation between 1996 and 2001. Patients were considered for VNS (Neurocybernetic Prosthesis system, Cyberonics, Inc.) if they had a minimum of two disabling seizures per month and disconcordant or non-localising clinical, EEG and imaging data. High intensity stimulation was used: signal on-time 30 seconds, signal off-time 5 minutes, pulse duration 500 milliseconds and frequency 30 Hertz. Output current was stepped up at 0.25 mA intervals up to a maximum of 2.5 mA. The patients were reviewed monthly initially for six months and then at regular intervals. The primary outcome was the percentage reduction in frequency of disabling seizures which involved loss of consciousness.

Results
Thirteen patients were implanted; all suffered from disabling refractory epilepsy resistant to high dosages of anti-epileptic drugs. Mean duration of treatment was 47.4 months and longest follow up was 71 months. Mean baseline seizure frequency was 26.6 seizures per month. The mean percentage reduction in convulsions were 33.2%, 47.1% and 40.0% at 6, 12 and 18 months respectively. One patient became seizure free and six (46%) had 50% or more reduction in seizure frequency. Response was poor (<20% reduction) in five patients (39%), leading to removal of the device. Seven patients in this series reported minor adverse events.

Discussion
In these patients with highly resistant seizures there was a significant reduction in seizure frequency which was sustained over a long period; however only one became seizure free. Implantation was uneventful and the generator was well tolerated.

Tolosa-Hunt Syndrome – A Clinical and Neuroradiological Correlation

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Background
Tolosa-Hunt syndrome (THS) is a syndrome of painful ophthalmoplegia with associated cranial nerves palsies that improves with corticosteroid therapy. Magnetic Resonance Imaging (MRI) of the brain is the preferred neuroimaging method with its better characterization and localization of the disease process to cavernous sinus/orbital apex. Our aim is to study the relationship between clinical presentation and progress with serial MRI findings.

Methods
Patients were identified by discharge diagnostic coding and registry from Department of Medicine/Radiology during the period January 1996 to January 2003. Subjects satisfied the International Headache Society criteria for THS were included. Medical records were systemically analyzed for clinical and neuroradiological findings.

Results
Nine subjects (eight female, mean age 54) were included. Systemic examination and blood tests were unremarkable in all patients. The oculomotor nerve was most common affected (66%), followed by the abducens (56%), ophthalmic branch of trigeminal (33%) and the trochlear nerve (11%). Computed tomography of the brain was done in six patients with abnormal enlargement of the symptomatic cavernous sinus found in two (33%) patients. MRI of the brain was done in all patients. Symptomatic cavernous sinus abnormalities were noted in eight (89%) patients with convex enlargement of the cavernous sinus which was iso-intense on T1 and proton weighted images, showed intense gadolinium
enhancement, with extension into contagious regions. In one patient the diagnosis was uncertain and biopsy was performed and was non-specific. She had gradual recovery clinically and neuro-radiologically three months later. The remaining eight (89%) patients received corticosteroid therapy. The median duration of treatment was 23 weeks. Six patients (66%) had complete recovery with resolution of MRI abnormalities. Three patients had partial response with residual neurological deficit despite MRI improvement.

Conclusion
In the appropriate clinical setting, MRI findings are very useful in the diagnosis of Tolosa-Hunt syndrome and follow-up for the response to corticosteroid therapy.

Status Epilepticus in 77 Patients

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Background
This study presents a retrospective review of the etiology, clinical features, and outcome of status epilepticus (SE) in 77 patients. Predictive factors of poor outcome in these patients were also identified.

Patients and Methods
All patients admitted between October 1999 and August 2003 to Caritas Medical Centre were identified if they satisfied the operative diagnosis of SE, which is defined as two or more epileptic seizures without full recovery of consciousness between attacks or continuous seizure lasting more than 10 minutes.

The medical records of these patients were reviewed to obtain the demographic data, clinical features, etiology, and outcome of patients, which was defined as “good” (unchanged from baseline or independent living) or “poor” (death, or ADL totally dependent).

Results
77 patients satisfied the inclusion criteria of SE. Seventy-three percent of them belonged to the elderly group (age above sixty-five years). The three leading etiologies for SE were cerebral infarctions (23), intracranial hemorrhage (13), and anoxia (11). Eighty-three percent of them had generalized tonic-clonic seizures. Forty-two percent of the patients had poor outcomes.

Using univariate analysis, increasing age (p=0.003), female sex (p=0.016), seizure duration longer than one hour (p=0.018), anoxia (p<0.001), need of ventilator care (p<0.001), history of terminal malignancy (p=0.001) were all associated with poor outcomes. Cerebral infarction was associated with good outcomes (p=0.083).

Using logistic regression, the three independent predictors of poor outcomes were increasing age (OR=0.94, p=0.003), female sex (OR=0.28, p=0.030), seizure duration longer than one hour (OR=3.43, p=0.036). Cerebral infarction as the etiology for SE was associated with good outcomes (OR=0.18, p=0.011).

Conclusions
SE is associated with high mortality and morbidity. The most common causes of SE in an elderly population were cerebrovascular disease and hypoxia brain damage. Increasing age, female sex and increased seizure duration were predictors of poor outcomes while cerebral infarction was associated with good outcomes.

Large Middle Cerebral Artery Infarction

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Background
The middle cerebral artery (MCA) and its branches are the most commonly affected brain vessels in cerebral infarction. Patients with large MCA infarct usually present with the total anterior circulation infarction (TACI) syndrome and suffer relatively poor prognosis. Despite documentation of such patients in local stroke registries, detailed report is not available from local Chinese patients.

Method
24 consecutive Chinese patients with clinical features of TACI were entered into this prospective descriptive study.

Results
The 30 day mortality rate was 21% and the 90 day mortality rate was 29%. 15 patients (63%) were dependent and were still staying in hospital or nursing home at 90 day but 2 patients (8%) had excellent recovery despite the severity of symptoms initially. Twelve patients (50%) had atrial fibrillation but only 1 of them was on anticoagulation before the development of stroke. 29% (n=7) had CT brain done within 3 hours of onset of stroke but all were not eligible for intravenous thrombolytic therapy because of the presence of early change in the scans. However, 46% (n=11) could have CT scan done within 3 to 6 hours of onset of stroke and 4 patients in this subgroup could be eligible for intraarterial thrombolytic therapy.

Conclusion
Large MCA infarction represents a subgroup of patient with a poor prognosis, although good recovery is still possible in a small minority of patients. Atrial fibrillation appears to be an important risk factor but prophylactic anticoagulation was severely underutilized. Intraarterial thrombolytic therapy may be explored to prevent the development of large MCA infarction in some patients presenting with the TACI syndrome.

Myopathic Changes Associated with Severe Acute Respiratory Syndrome (SARS)

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Background
The global outbreak of the Severe Acute Respiratory Syndrome (SARS) has resulted in significant morbidity and mortality. Weakness and raised creatine kinase are common features encountered in clinical practice. The nature and cause of myopathy associated with SARS infection remain uncertain because there has been no report of histological or post-mortem examination of the skeletal muscle.

Methods
Patients who were diagnosed SARS based on the World Health Organization (WHO) case definition criteria of “probable case” and who underwent a post-mortem examination in March and April 2003 were included. All had radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome on chest X-ray, and with autopsy findings consistent with the pathology of RDS without an identifiable cause.

Post-mortem skeletal muscles from 8 consecutive patients who died from SARS in March 2003 were studied under light and electron microscopy, and immunohistochemistry.
Results
Among the 8 cases recruited, 7 cases were from Prince of Wales Hospital, and the remaining case was from Princess Margaret Hospital. All developed SARS pneumonitis, and artificial ventilation was required in six except two, who were treated conservatively due to poor pre-morbid state and concurrent lung cancer respectively. All eventually died from respiratory failure. Focal myoﬁber necrosis was identiﬁed in four out of eight cases. Macrophage inﬁltration and regenerative ﬁber were scanty. Signiﬁcant atrophy of type II myoﬁbers was noted in all 4 patients who received steroid. Viral cultures for coronavirus and examination for viral particle under electron microscopy were performed in two patients and both were negative.

Conclusion
There is a spectrum of myopathic changes associated with SARS infection. Focal myoﬁber necrosis is common and possibly is immune-mediated. Critical illness myopathy with superimposed steroid-induced myopathy may also play an important role in some patients.

Study on Circadian Rhythm of Stroke and Stroke Severity
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Background and hypothesis
Circadian rhythm in stroke occurrence had been established. We hypothesize that more cerebral damage from stroke occurs more likely at peak of the rhythm due to changes in underlying physiological variables.

Methods
Retrospective review of 590 patients admitted for stroke to a tertiary hospital from 1 August 2002 to 28 February 2003. Time of stroke occurrence was categorized into four 6-hour periods. Patients in each category were compared for their average NIHSS score.

Results
Time of stroke onset was known in 528 patients. Circadian rhythm of stroke onset was demonstrated for ischaemic stroke (n = 477) which had peak at 06:00-11:59 and trough at 00:00-05:59, with statistically signiﬁcant difference. Similar pattern was observed for hemorrhagic stroke (n = 61) but the difference was not statistically signiﬁcant. The overall mean or median NIHSS score in each patient category by time period did not differ signiﬁcantly between categories, even when patients were stratified according to stroke pathology (cerebral hemorrhage / ischaemia), or occurrence of atrial ﬁbrillation. Independent predictors of higher stroke severity were identiﬁed, which included female gender, high pre-stroke Rankin score, presence of atrial ﬁbrillation on admission, and hemorrhagic stroke.

Conclusions
Circadian rhythm of ischaemic stroke occurrence was demonstrated, which had peak at 06:00-11:59 and trough at 00:00-05:59. There was no signiﬁcant association of severity of ischaemic or hemorrhagic stroke with stroke onset time or circadian rhythm of stroke occurrence.

Possible Involvement of CNS by the Human Coronavirus of Severe Acute Respiratory Syndrome (SARS) – Case Report
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A 32-year-old woman has contracted severe acute respiratory syndrome (SARS) in March 2003. She was also pregnant in her second trimester. She had fever, chills, rigor and her Chest X ray showed patchy consolidations over right upper lobe and both lower lobes. After admission she was treated with ribavirin 500 mg tid and hydrocortisone 100 mg q6h. Her condition rapidly became worsened and was electrically ventilated by day 7. Lower segment caesarean section was performed and a baby girl was born. Her renal function deteriorated since day 8 with creatinine increased to 504 umol/L, and she required hemodialysis. The diuretic phase occurred on day 19. On day 22 she had a generalized tonic-clonic convolution with up-rolling eyeballs lasting for a minutes. There was no neck rigidity and no neurological deﬁcit. Lumbar puncture showed an opening pressure of 15 cm, with free ﬂow of clear CSF. The CSF protein was 0.38 g/L, and the glucose was 5.1 mmol/L against serum glucose of 6.6 mmol/L. Microscopy showed that WBC of less than one per cc, and gram stain, bacterial cultures and viral cultures were negative. RT-PCR on CSF for SARS-coronavirus was positive. Later the EEG and MRI brain showed no abnormalities. IgG antibody titer to SARS-coronavirus by immunoflourescence assay was <1:25 on day 1 and was 1:1600 on day 39. In addition to CSF, RT-PCR for SARS-CoV was positive in stool and peritoneal ﬂuid.

This patient has generalized convulsion with a positive RT-PCR for SARS-CoV in the CSF suggests infection of the central nervous system by SARS-coronavirus. Cerebral hypoxaemia was unlikely as she was closely monitored in ICU and there was no such record of hypoxaemia. Acute renal failure was unlikely as the renal function has been improving. Electrolyte and acid-base disturbances were absent. There was no hypertension or proteinuria to suggest eclampsia. Ribavirin has not been reported to cause convulsion and it would be very unlikely for the event to occur 5 days after discontinuation of this drug. The patient declined another lumbar puncture to test for CSF for RT-PCR, and the presence of SARS-coronavirus in the CNS cannot be ﬁrmly established.

Our case demonstrates that SARS-CoV can possibly infect multiple organs and systems.

Predicting Prognosis After the First Stroke in the Chinese Population
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Objective
To identify the factors that predict a poor outcome after the first episode of acute stroke among Chinese in Hong Kong.

Methodology
All patients admitted to a local hospital with a first-in-a-lifetime stroke from 1st February 2001 to 30th June 2001 were reviewed. Potential factors that would predict a poor outcome at 3 months, according to the Modiﬁed Rankin scale with a score of >3 or death, were noted. These included age, sex, pre-morbid Rankin’s scale, risk factors for stroke, baseline variables, fasting blood results, National Institute of Health stroke scale (NIHSS) and CT ﬁndings.

Results
19.8% (44 out of 221 patients) of cerebral infarction patients and 56% (28 out of 50 patients) of intracerebral haemorrhage patients had a poor outcome at 3 months. After multivariate analysis, the factors associated with a poor outcome in the cerebral infarction group included age (adjusted odds ratio = 1.08, 95% conﬁdence interval 1.03-1.13, p = 0.001), admission NIHSS score (adjusted odds ratio = 1.18, 95% conﬁdence interval 1.10-1.27, p < 0.0001) and incontinence on admission (adjusted odds ratio = 16.32, 95%
confidence interval 2.35-113.45, \( p = 0.005 \). For the intracerebral haemorrhage group, the factors that predicted a poor outcome were age (adjusted odds ratio = 1.10, 95% confidence interval 1.01-1.19, \( p = 0.02 \)) and admission NIHSS score (adjusted odds ratio = 1.34, 95% confidence interval 1.13-1.58, \( p = 0.001 \)).

Conclusions
Age and admission NIHSS score were associated with a poor stroke outcome in both cerebral infarction and haemorrhage patients. For cerebral infarction, incontinence on admission could also predict a poor outcome.

Epidemiology of First Ever Generalised Tonic-clonic Seizures in Adults: A Prospective Study

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Objective
To describe the clinical characteristics and estimate the incidence of first generalised tonic-clonic seizures (GTCS) among adults in Kwan Tong region in Hong Kong.

Methods
In Hong Kong, patients presenting to the emergency department with a first ever GTCS are routinely admitted into hospitals for investigation and treatment. The study was conducted in the only acute hospital with emergency service in Kwan Tong region which has a population of 562,427, of whom 479,188 are 15 years or above. The region has the second highest proportion (14.5%) of the elderly population (65 years or above) in Hong Kong. We prospectively screened the records of all patients admitted to the six main acute medical and geriatric wards within 48 hours of admission and determined whether epileptic seizures were the presenting complaints. Patients admitted for the first GTCS were included in the analysis.

Results
Between 1 March 2002 and 28 February 2003, there were 24,259 admissions via the emergency department to all medical or geriatric wards of the hospital. Among them, 567 (2.3%) were discharged to 15.5 to 62.5 per 100,000 for ages 15 - 34 years, 35 - 64 years, and 65 years or above, respectively (\( p < 0.001 \)).

The seizure/epilepsy types were classified as acute symptomatic in 21%, remote symptomatic in 48%, cryptogenic in 21%, idiopathic in 2% and unclassifiable in 8%. The commonest aetiology was stroke, accounting for 44% among the whole cohort, or 76% among those 65 years or above.

Conclusion
The annual incidence of first GTCS among population 15 years or above was estimated to be 22.1 per 100,000. Twenty-one percent were acute symptomatic in nature. Stroke is the commonest aetiology identified, likely accounting for the highest incidence among the elderly compared with other age groups in the region.

Cerebral Palsy – Correlation of Functional Assessment with Risk Factors

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Objective
To study the functional status of cerebral palsy (CP) using Functional Independence Measure for Children (WeeFIM) and its correlation with risk factors.

Methods
A cross-sectional study of 76 CP children was conducted with a validated instrument for rehabilitation (Chinese WeeFIM). This is an 18-item ordinal scale which measure a child’s consistent performance in daily functional skills in 3 domains (self-care, mobility, and cognition). This is assessed by interviewing / observing a child’s performance of a task and referenced to criterion standards. The interview will take only 5-10 minutes. The scores ranged from 1 to 7 (1 = total assistance, 2 = maximal assistance, 3 = moderate assistance, 4 = minimal contact assistance, 5 = supervision, 6 = modified independence and 7 = complete independence). Thus, the total score is 126.

Results
The mean age of our CP cohort was 12 years. The male to female ratio was 2.5:1. The mean total WeeFIM score was 80.7 (mean total quotient = 67.21%). The mean sub-scores / quotients for self-care, mobility and cognition were 35.7 / 67.9%, 21.8 / 62.6% and 23.2 / 69% respectively.

The best functional status occurred in the hemiplegic group (14), and the worst being tetraplegia (12). Children with diplegia (27), ataxia (5), dyskinesia (14) and mixed (4) scored in-between.

The degree of functional dependency was associated with (i) mental retardation (\( p = 0.012 \)), (ii) epilepsy (\( p = 0.006 \)), (iii) type of CP (\( p < 0.001 \)) and (iv) the severity status using Gross Motor Function Classification (GMFCS) (\( p < 0.001 \)).

Conclusion
Regular assessment of the achievement of functional independence is important for targeting therapeutic goals in any multidisciplinary rehabilitation program. Significant correlation with dependence or assistance was found with the type, severity, and associated co-morbidities of CP children. For any child with CP, regular monitoring with a simple tool for the achievement of functional independence is worthwhile for both early training and later educational needs.

Topiramate-Valproate-induced Hyperammonemnic Encephalopathy Syndrome (TV-HES) – Case Report

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A 15.5-year-old boy with chromosomal abnormality [inversion duplication of chromosome 15], having severe mental retardation, intractable generalized epilepsy and behavioral problems was admitted for acute onset of irritability, increasing sleepiness and worsening of seizures. He tolerated valproate in combination with other anticonvulsants. He was found to have hyperammonemia within 2 weeks after low dose topiramate was added to valproate. He recovered within 7 days after discontinuation of valproate. Topiramate was tailed off. The reintroduction of valproate, monotherapy caused hyperammonemia again without clinical features of encephalopathy. He also developed Anticonvulsant Hypersensitivity Syndrome (AHS) when phenytoin was used. We propose the term of Topiramate-Valproate-induced Hyperammonemic Encephalopathy Syndrome (TV-HES) to include the following features: excessive sleepiness or somnolence, aggravation of seizures, hyperammonemia, and absence of triphasic waves in EEG in any individual on simultaneous Topiramate-Valproate
therapy. Other rarer reported features include normal to slightly deranged liver enzymes or thrombocytopenia. The ammonia level ranged 1.5 to 2 times normal. The serum valproate level might be within the therapeutic range. The possible mechanism is Topiramate-induced aggravation of all the known complications of mono-Valproate therapy. This condition is reversible with stopping of either valproate or Topiramate.

Isolated Recurrent Idiopathic Transverse Myelitis

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Background
Idiopathic transverse myelitis (TM) is most commonly due to immune-mediated inflammatory demyelination of the spinal cord as a parainfectious phenomenon. Known causes of recurrent TM include connective tissue diseases such as lupus, multiple sclerosis and Devic’s disease and antiphospholipid antibody syndrome. Isolated recurrent idiopathic TM is rare and exact etiology and predictive factors for recurrence are uncertain.

Methods
All patients with transverse myelitis managed in our hospital from 1998 to 2001 were studied. Those with multiple sclerosis, Devic’s disease, lupus and other known causes of TM were excluded. Clinical, biochemical and radiological features were analyzed. All patients were followed up for at least 2 years.

Results
A total of 16 patients with idiopathic TM were studied. Four patients had recurrent attacks with interval of 1 to 4 months between attacks while the other 12 patients had one attack only. All patients with recurrent TM were female while 5 of the 12 with single attacks were men. All patients with recurrent TM had MRI documented signal changes affecting 3 or more vertebral segments longitudinally with cord swelling while only 2 of the 12 with single attack had such extensive lesion and just 1 had cord swelling. All the recurrent cases were negative for oligoclonal band in cerebrospinal fluid while 50% of the single-attack group harbored oligoclonal band. Neurological recovery was unfavourable for the recurrent group while most of the non-recurrent patients could walk independently.

Conclusion
Idiopathic recurrent transverse myelitis seems to be characterized by a female predominance, longitudinally extensive cord lesion with swelling, absence of oligoclonal band and poor prognosis. An autoimmune basis should be considered.

Recurrent Headache in Children – A 3 Years’ Hospital-based Study (2000-2002)

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Background
The prevalence of headache in Caucasian children was estimated to be 37-51% (age=7 years); and 57-82% by age 15 years. There is no local data on the prevalence of recurrent headache in Chinese children in Hong Kong.

Objective
To study the pattern of recurrent headache in children in a general out-patient setting of a tertiary hospital.

Method
A retrospective medical record review was performed for children <18 years with ICD coding of headache in the general out-patient clinic of Queen Mary Hospital in the Department of Paediatrics and Adolescent Medicine over a 3 years period (2000-2002). After reviewing the records, we reclassify the subtypes according to the 2nd version diagnostic criteria of the International Headache Society (IHS) 2004. The demographic data, family history, neuro-imaging studies and associated comorbidities were analyzed.

Results
Altogether, 136 cases were retrieved. The mean age of presentation was 10.73 years. The initial coding was migraine in 14 (ICD 346.90), tension headache in 32 (ICD 307.81) and headache in 90 (ICD 784.00). After reclassification using IHS criteria, the subtypes of migraine, tension or unclassified headache were 11 (8 %), 31 (23 %) and 94 (69 %) respectively. There was no statistically significant difference for the mean age of onset for migraine, tension or unclassified headache (11.4±2.2, 9.2±3.9 and 9.4±3.7 years) respectively. A positive family history of migraine/headache was present in 36.4%, 51.6% and 36.2% of migraine, tension and unclassified headache respectively. There was a predominance of males in all 3 types of headache, with male to female ratio for migraine being 2.7:1 while that for tension headache was 1.38:1 and 1.24:1 for unclassified headache. Again, no statistically significant difference could be found in these 2 parameters.

Neuroimaging studies (CT scan and/or MRI) were performed in 39 cases (28.7%). Only 4 cases (4 CT and 2 MRI) revealed abnormalities. CT abnormalities include arachnoid cyst, hypodensity at right cranial fossa, retrocerebellar arachnoid cyst and mildly dilated third ventricle. MRI abnormalities include pineal cyst and occipital white matters changes. EEG was performed in 16 cases (11.8%) with abnormalities found in 5 cases: generalised epileptic discharge, mild left cerebral dysfunction, epileptic foci in right occipital region, focal discharges over right posterior area and right central temporal spikes.

Comorbidities: The co-occurrence of abdominal pain and migraine was 18.2% while that for tension and unclassified headache was 22.6% and 20.2% respectively. 7.7% girls with tension headache and 7.1% girls with unclassified headache also had dysmenorrhoea. However no girls have both migraine and dysmenorrhoea. Other pain pattern found in children with recurrent headache include low back pain, limb pain and chest pain.
Conclusions
Children with headache may not present as the typical headache pattern in adults. While the IHS criteria was developed primarily for headache disorders in adults, the number of tension headache and migraine may be underestimated in our study. A longer follow-up period is required for establishing a definite diagnosis for the type of headache in children. Males are more affected than girls. This was consistent with Caucasian’s data. Co-occurrence of other pain symptoms was commonly seen in our children.

References

Spinal Muscular Atrophy (SMA) – Natural History and Functional Status in Hong Kong Children

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Objective
To study the natural history and current functional status of children with SMA in Hong Kong.

Methods
A SMA Registry had been collected since 1984 in Duchess of Kent Children’s Hospital. Families of SMA (FSMA) has been established in 2000. A total 102 SMA cases had been collected. We analyzed 81 SMA cases (34 males; 47 females) with clinical information available in September 2002. SMA cases were classifying according to classification of the International SMA Consortium. SMA type III was further classified into IIIa (onset <3 years) and IIIb (>3 years). The validated Chinese Functional Independence Measure for Children (WeeFIM) was administered to 39 active SMA cases to assess their performance in daily functional skills in 3 domains (self care, mobility and cognition).

Results
Our SMA Registry consisted of type I (severe) = 20 (24.7%); type II (intermediate) = 26 (32.1%) and type III (mild) = 35 (43.2%).

The survival probability for SMA I was 55%, 40%, 30%, 30%, for type II was 100%, 100%, 100%, 92%, 88% at 1, 2, 4, 10, and 20 years of age respectively.

The probability of being ambulatory (defined as walking with or without assistance) at 2, 4, 10, 20 years of age for SMA II was 64%, 59%, 32%, 5%; and 100%, 100%, 82%, 71% for type IIIa; and 100%, 100%, 89%, 67% for type IIIb.

WeeFIM score: The total scores were 30 (N=4; mean total quotient = 24%), 72 (N=15; mean total quotient = 57%), 94 (N=9; mean total quotient = 75%) and 97 (N=11; mean total quotient = 78%) for types I, II IIIa and IIIb respectively.

For the domain of mobility, more than 90% of type I, II, IIIa and 63% of those with type IIIb required assistance. Around 55% SMA type IIIa and b cases attained functional independence in both self-care and cognition domains.

Conclusion
The natural history of progression for Chinese SMA patients was similar to the Caucasians. Knowledge on the prognosis such as long term survival and functional status is important for counseling.

Survival probability in SMA types I and II and probability of being ambulatory for SMA types II, IIIa and IIIb

<table>
<thead>
<tr>
<th>SMA type</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>10</th>
<th>20</th>
<th>40</th>
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</thead>
<tbody>
<tr>
<td>I (N=20)</td>
<td>55</td>
<td>40</td>
<td>30</td>
<td>30</td>
<td>—</td>
<td></td>
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<tr>
<td>II (N=29)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>92</td>
<td>88</td>
<td>85</td>
</tr>
<tr>
<td>Probability of being ambulatory at a certain age (%)</td>
<td>64</td>
<td>64</td>
<td>59</td>
<td>32</td>
<td>5</td>
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</tr>
<tr>
<td>IIIa (N=17)</td>
<td>100</td>
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Acknowledgement
Mrs Fok Mei Ling (Director of FSMA)

Valproate-induced Hyperammonemic Encephalopathy

L. Y. Chan, A. C. F. Hui, K. S. Wong
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Background
Valproate-induced hyperammonemic encephalopathy is uncommon with less than 30 cases reported on Medline Search. We review the clinical, EEG and magnetic resonance spectroscopy findings in a patient with this condition.

Case
A 35-year-old man had left parietal oligodendroglioma with debulking surgery done in 1997. He later underwent a second operation with postoperative radiotherapy in 2001 because of tumour progression. Because of a generalized tonic-clonic convolution, he was put on valproate 800 mg Q6H intravenously. After two days on this regime he developed impaired consciousness. Urgent CT brain did not show evidence of tumour relapse but the EEG revealed diffuse slow waves at 3–4 Hz. Valproate level was 680 umol/L, phenobarbitone 175 umol/L and ammonia level was 85 umol/L (upper limit 47 umol), rising to 113 umol/L on the next day, along elevated live enzymes. The valproate dosage was reduced to 300 mg Q8H, after which the patient’s improved markedly over two days with normalization of both liver function and EEG. MRI and MR spectroscopy later both showed no evidence of tumour relapse or congenital urea cycle disorders.

Conclusion
Asymptomatic hyperammonaemia is a recognized feature of chronic use of valproate. The mechanism is not completely understood but is probably related to the inhibition effect of ammonia on glutamate metabolism of astrocytes; this leads to intracellular accumulation of glutamate and subsequent osmotic cellular swelling. In cases sufficiently severe to cause encephalopathy, the ammonia level is usually >100 umol as in our patient. However, our patient is particular susceptible to the development of encephalopathy because of multiple factors underlying including history of brain surgery and concomitant phenobarbitone administration and valproate induced deranged liver function which delayed the clearance of ammonia. But the rapid improvement with reduction of valproate in this case highlights the importance of recognising this complication.

Case Report: The First Reported Case of Intracranial Vertebral Artery Angioplasty in Hong Kong

W. C. Fong1, Y. L. Cheung2, K. W. Tang2, K. M. Cheng1, J. H. M. Chan1, P. C. K. Li1

Acknowledgement
ACFH (Head of Departments of Medicine and Radiology, Prince of Wales Hospital)

References
Background
Angioplasty had been performed as the treatment for vertebrobasilar atherosclerotic disease in overseas centres. It was first reported in 1993. However such intervention is still associated with severe procedure related complications nowadays. The selection of patients for such intervention is difficult in view of poorly defined risk and benefit ratio.

Method
Case report.

Results
A 61-year-old man with history of chronic smoking and hypertension, was admitted for dizziness and right hemiplegia due to left brainstem infarct. Subsequently he presented with 2 episodes of postural related “lock in” syndrome. Then he complained of persistent postural related dizziness afterward. MR angiogram and the subsequent cerebral angiography confirmed the diagnosis of severe vertebrobasilar insufficiency. Severe stenosis was noticed in right vertebral artery beyond the right PICA while there is complete occlusion in left vertebral artery beyond the left PICA. Basilar artery was underfilled and both posterior cerebral arteries were not seen. The patient’s symptoms failed to respond to conservative treatment. Then angioplasty was performed to the right intracranial vertebral artery under general anaesthesia. Post angioplasty angiography showed opening up of the stenotic segment of right vertebral artery with good flow to bilateral posterior cerebral arteries. The patient recovered with no new neurological deficit and his postural related dizziness was subsided after the angioplasty.

Conclusions
With the advances of percutaneous interventional device, such intervention can be performed with acceptable complication rate. This case report illustrated how it could be successfully performed in a patient who suffered from severe vertebrobasilar insufficiency, refractory to the medical therapy.
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