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21st Annual Scientific Meeting of The Hong Kong Neurological Society, 15–16 November 2008

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# SCIENTIFIC PROGRAMME

VENUE: HOTEL SHANGRI-LA, KOWLOON

15 NOVEMBER 2008, SATURDAY

09:00 – 09:30	Registration
09:30 – 10:50	<b>FREE PAPER PRESENTATIONS (1)</b> <i>Chairpersons: PW Ng, WC Fong</i>
10:50 – 11:10	Coffee Break / Poster Viewing
11:10 – 11:30	<b>FREE PAPER PRESENTATIONS (2)</b> <i>Chairpersons: KK Lau, YF Cheung</i>
11:30 – 12:30	<b>DISSERTATION HIGHLIGHTS</b> <i>Chairpersons: KK Lau, YF Cheung</i>
12:30 – 14:00	Lunch / Press Conference
14:00 – 14:10	<b>WELCOME REMARK</b> <i>TH Tsoi</i>
14:10 – 15:20	<b>ALLERGAN SYMPOSIUM ON MOVEMENT DISORDERS</b> <b>JOINT SYMPOSIUM WITH THE HONG KONG MOVEMENT DISORDER SOCIETY</b> <i>Chairpersons: Jonas Yeung, KL Tsang</i>  <b>The Updates of Managing Cervical Dystonia/Movement Disorders with Botulinum Toxin</b> <i>Han-cheng Wang</i>  <b>Basal Ganglia Motor Dysfunctions: a Basic Scientist's Perspective</b> <i>Wing-ho Yung</i>
15:20 – 15:40	Coffee Break / Poster Viewing
15:40 – 17:00	<b>SYMPOSIUM ON NEUROIMMUNOLOGY</b> <i>Chairpersons: KH Chan, YL Yu</i>  <b>Neuromyelitis Optica</b> <i>Vanda A Lennon</i>  <b>Management of Multiple Sclerosis in Asian Perspective</b> <i>Patrick Li</i>

**16 NOVEMBER 2008, SUNDAY**

<b>09:00 – 09:30</b>	<b>Registration</b>
<b>09:30 – 10:50</b>	<b>SYMPOSIUM ON STROKE</b> <b>JOINT SYMPOSIUM WITH THE HONG KONG STROKE SOCIETY</b> <i>Chairpersons: Raymond Cheung, CY Huang</i> <b>Acute Stroke Care Pathway in Hong Kong West Cluster</b> <i>Raymond Tak-fai Cheung</i> <b>A Novel Treatment Modality for Intracerebral Aneurysm</b> <i>Wai-man Lui</i> <b>Endovascular Treatment for Ischaemic Stroke</b> <i>Thomas Leung</i>
<b>10:50 – 11:10</b>	<b>Coffee Break / Poster Viewing</b>
<b>11:10 – 12:30</b>	<b>SYMPOSIUM ON NEUROIMAGING</b> <i>Chairpersons: Vincent Mok, Richard Kay</i> <b>Imaging of Epilepsy</b> <i>Henry Mak</i> <b>Neuroimaging in Cerebrovascular Diseases</b> <i>Wynnie WM Lam</i> <b>PET Scans in Alzheimer's Disease and Parkinsonism</b> <i>Eric Leung</i>
<b>12:30 – 14:00</b>	<b>Lunch</b>
<b>14:00 – 15:30</b>	<b>SYMPOSIUM ON EPILEPSY</b> <b>JOINT SYMPOSIUM WITH HONG KONG EPILEPSY SOCIETY</b> <i>Chairpersons: Patrick Kwan, Colin Lui</i> <b>Diagnosis and Differential Diagnosis of Epileptic Seizures and Epilepsy</b> <i>Shih-hui Lim</i> <b>Treatment of Epilepsy in Patients with Comorbidities</b> <i>Chong-tin Tan</i> <b>The Hong Kong Epilepsy Guideline</b> <i>Jason KY Fong</i>
<b>15:30 – 15:50</b>	<b>Coffee Break / Poster Viewing</b>
<b>15:50 – 17:00</b>	<b>SYMPOSIUM ON GENERAL NEUROLOGY</b> <i>Chairpersons: Edmund Woo, YW Chan</i> <b>Genetics for Neurologists: DNA-based Diagnosis of Neurogenetic Disease</b> <i>Ching-wan Lam</i> <b>Neurotoxicology</b> <i>Thomas YK Chan</i> <b>Attention-Deficit/Hyperactivity Disorder</b> <i>Sophelia HS Chan</i>

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14 Nov 2008 – 1st Annual Scientific Meeting of The Hong Kong Movement Disorder Society – Workshop  
on Botulinum Toxin Injection  
Queen Elizabeth Hospital  
17 Nov 2008 – A Refresher Course in Improving EEG Reading and Interpretation Skills  
Queen Elizabeth Hospital  
22 Nov 2008 – ASEPA-ASNA EEG Certification Part 1 Examination  
Queen Elizabeth Hospital

## The Validity, Reliability and Utility of the Cantonese Montreal Cognitive Assessment (MoCA) in Chinese Patients with Confluent White Matter Lesions

Adrian Wong<sup>1</sup>, Pauline Kwan<sup>1</sup>, Anne Chan<sup>1</sup>, Wynn Lam<sup>2</sup>, Ki Wang<sup>2</sup>, David Nyenhuis<sup>3</sup>, Ziad Nasreddine<sup>4</sup>, Lawrence Wong<sup>1</sup>, Vincent Mok<sup>1</sup>

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<sup>3</sup> Department of Neurology and Rehabilitation Medicine, University of Illinois at Chicago, Center for Stroke Research, Chicago, USA

<sup>4</sup> Center for Clinical Research, Neurology Service, Hôpital Charles LeMoyné, Quebec, Canada

**Background:** The Montreal Cognitive Assessment (MoCA) is a brief screening test useful in detecting mild cognitive impairment in non-stroke Caucasian samples. However, its (1) concurrent validity against formal neuropsychological measures; (2) external validity in patients with confluent white matter lesions (WML); and (3) utility in Chinese patients, have not been investigated.

**Methods:** Thirty-three patients (mean age, 70.9 years; education, 5.6 years) with confluent WML with no-to-mild cognitive impairment (CDR 0 in 27%; 0.5 in 73%; mean MMSE, 25.3) and 33 matched stroke-free, cognitively healthy controls (mean age, 68.1 years; education, 7.2 years; MMSE, 28.0) were recruited from our neurology clinic and administered the Cantonese MoCA and a neuropsychological battery consisting tests of executive and general cognitive functions. Concurrent validity against cognitive domain composite scores was assessed using linear regression analyses. Receiver operating curve (ROC) was constructed to evaluate the ability of the MoCA in differentiating patients from controls. Two-week test-retest and intra-rater reliability were examined in 17 and 14 subjects, respectively.

**Results:** Both executive ( $\beta=0.349$ ,  $P<0.001$ ) and non-executive ( $\beta=0.823$ ,  $P<0.001$ ) domain composite scores significantly predicted the Cantonese MoCA total score after adjusting for age, sex, education and geriatric depression scale. It effectively differentiated patients from controls (area under ROC=0.861). A cutoff of  $\leq 21$  offers an optimal balance of sensitivity (82%) and specificity (73%) with acceptable negative (75%) and positive (80%) predictive values. Test-retest and intra-rater reliability were high (intraclass correlation coefficient=0.944 and 0.877, respectively, both  $P<0.001$ ). The Cantonese MoCA was well accepted by most subjects.

**Conclusion:** The Cantonese MoCA is a psychometrically valid and reliable cognitive screening instrument for use in Chinese patients with confluent WML.

## The Clinical, Electrophysiological Features of Guillain-Barré Syndrome in Hong Kong Chinese

Chi-nam Lee, Chun-ming Cheung, Sonny Fong-kwong Hon, Ka-lock Shiu, Mandy Man Auyeung, Richard Li, Sze-wai Yeung, Tak-hong Tsoi

Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

**Background:** The incidence, clinical and electrophysiological features of Guillain-Barré syndrome (GBS) are not well studied in our local population.

**Methods:** It is a retrospective study of all GBS patients of age  $>18$  from January 2006 to December 2007. We critically reviewed the hospital charts of all patients with systemic analysis of the demographics, clinical course, electrophysiological findings and laboratory results.

**Results:** Fifteen patients with GBS and its variants were identified. The incidence was 1.46 per 100 000. Twelve patients had acute inflammatory demyelinating polyradiculopathy (AIDP), three had Miller-Fisher variant confirmed by positive GQ1b antibody, no axonal variant was diagnosed. Male-to-female ratio was 4:1 with a mean age of 54 (range, 28-78) years. Ten (66.7%) patients had preceding events of either enteritis or respiratory tract symptoms. Weakness was the commonest symptom on presentation (100%), followed by numbness (33.3%), facial weakness (26.7%), ophthalmoplegia (20%), pain (6.7%), and autonomic dysfunction (6.7%). CSF protein was elevated in nine out of 10 patients (mean time of LP from onset, 6.3 days). All patients had nerve conduction study (NCT) performed (average, 5.5 days). Demyelinating neuropathy was demonstrated in 11 (73.3%) patients. Prolonged or absent F-wave response and decrease in conduction velocity were the commonest finding (60%). Eleven patients received intravenous immunoglobulin (IVIG) alone, three received IVIG and plasma exchange due to disease progression, one patient received no immunotherapy in view of mild impairment. The mean length of hospitalisation was 43 days (range, 8-220 days), no patient died. Ten (66.7%) patients had  $>1$  score improvement in the modified Rankin scale upon discharge. Four patients had significant disability upon discharge of modified Rankin scale  $>3$ .

**Conclusion:** The incidence and pattern of GBS in our present study is similar to western countries with comparable outcomes.

## Analysis of Cerebrospinal Fluid Findings and Clinical Features of Chinese Systemic Lupus Erythematosus Patients

Tsz-yan Lee, Shuk-yi Chau, Moon-ho Leung  
Queen Elizabeth Hospital, Hong Kong SAR

**Background:** The characteristics of cerebrospinal fluid (CSF) findings in systemic lupus erythematosus (SLE) patients, having central nervous system (CNS) infection, neuropsychiatrist SLE (NPSLE) or none of these, had not been widely described.

**Aim:** To describe the clinical features of SLE patients who had lumbar puncture (LP) performed in a single centre.

**Methods:** From January 2000 to June 2008, all such patients were identified using clinical records and microbiology laboratory database. All patients fulfilled the ACR Revised Criteria (1997) for the classification of SLE. NP manifestations were recorded using ACR NPSLE nomenclature and case definitions (1999). Central nervous system infection was defined as positive culture in CSF. Clinical and laboratory parameters were analysed by Mann-Whitney *U* Test.

**Results:** Thirty-six SLE patients had LP performed during this period. The mean age was 40 years and median duration of follow-up was 42 months. Fourteen patients had seizure, 12 acute confusional state, six focal neurological sign, and six psychosis at presentation. Twenty-one patients had manifestations attributable to NPSLE. Five patients had microbiological proof of CNS infection—one patient had *Listeria monocytogenes* and four patients *Mycobacterium tuberculosis*. Patients with SLE who had CNS infection had a higher CSF protein (median 0.75 g/L [IQR 0.45-5.1] vs 0.3 g/L [IQR 0.15-0.58],  $P=0.03$ ), a lower CSF glucose/blood glucose ratio (median 0.29 [IQR 0.18-0.38] vs 0.54 [IQR 0.36-0.64],  $P=0.01$ ) and a higher CSF white cell count (median  $19/\text{mm}^3$  [IQR 11-34] vs  $1/\text{mm}^3$  [IQR 1-2.5],  $P=0.002$ ) than those in NPSLE. However, five (24%) patients who had NPSLE had high CSF protein level ranging from 0.53 g/L to 2.27 g/L. There was no statistically significant difference in serum total white cell count, lymphocyte, C3 and anti-dsDNA at presentation between two groups. The use of prednisolone, cyclophosphamide, azathioprine and cyclosporin before the onset of CNS symptom were also similar between two groups.

**Conclusions:** Analysis of CSF may provide an important and rapid clue to differentiate NPSLE from CNS infection. However, high CSF protein may also be found in NPSLE.



## Characteristics and Long-term Outcome of First-ever Isolated Acute Transverse Myelitis

FP 5

Richard Li, Chi-nam Lee, Chun-ming Cheung, Sonny Fong-kwong Hon, Ka-lock Shiu, Mandy Man Auyeung, Sze-wai Yeung, Tak-hong Tsoi  
Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

**Background:** Results from western countries showed rate of development of multiple sclerosis (MS) from acute transverse myelitis (ATM) patients are around 30 to 50%. There is scanty of local data.

**Methods:** All patients presenting with ATM to us from July 1997 to June 2008 were included. The hospital records were retrospectively reviewed and clinical features, CSF findings and MRI of spinal cord and brain were systemically analysed. Treatment response and functional outcome (6 months after the event) of these patients were studied.

**Results:** Thirty-three patients with ATM were identified during the study period. The incidence of ATM was 0.6 per 100 000 person-years. After a mean follow-up of 42.9 months, 30.3% (10/33) of patients developed neuromyelitis optica (NMO)/MS. Among 22 patients with monophasic disease, the median age of onset was 44 (range, 12-89) years with 16 females. Nineteen (86.4%) patients were idiopathic, and three (13.6%) patients were related to lupus. Three patients have positive oligoclonal bands. 77.3% (17/22) of patients had myelitis involvement of more than three vertebral segments longitudinally in MRI. Two patients died, seven (31.8%) patients had poor outcome (mRS, 3-5) and 13 patients (59.1%) had good outcome (mRS, 0-2) 6 months after the event. For the group of patients developing recurrent disease (n=11), four (36.4%) patients and six (54.5%) patients fulfilled the diagnostic criteria of NMO and classical MS respectively. One patient had recurrent myelitis and later found to have underlying diffuse large B-cell lymphoma. Four patients were female. Only one NMO patient had positive oligoclonal band. The interval time for first episode to definite MS ranged from 4 months to 9 years.

**Conclusion:** Majority of monophasic ATM patients have good recovery. 30.3% developed NMO and MS. Risk of progression is similar to Caucasian population.

## Nerve Conduction Study for Hereditary Neuropathy with Liability to Pressure Palsies

FP 6

Raymond Chun-kong Chan, Bun-hey Fung, Ping-wing Ng  
United Christian Hospital, Hong Kong SAR

**Background:** Hereditary neuropathy with liability to pressure palsies (HNPP) is a rare autosomal dominant inherited disorder mainly due to 1.5 megabase deletion in chromosome 17p11.2-p12 where the PMP-22 gene is located. Patients commonly present with recurrent episodes of nerve palsy after trivial unnoticed trauma or prolonged pressure, particularly at the anatomic entrapment sites. Electrophysiological studies often show generalised neuropathy with prolonged distal motor and sensory latencies together with non-uniform slowing of conduction velocities at usual sites of nerve compression.

**Methods:** Three patients with HNPP were evaluated by nerve conduction studies. All have confirmation of their diagnosis by genetic tests. The neurophysiology results were reviewed.

**Results:** The patients presented with either: (1) episode(s) of transient nerve palsy with nearly complete clinical recovery; or (2) asymptomatic course. The nerve conduction studies, however, revealed typical changes of prolonged distal motor latencies and slowed conduction velocities.

**Conclusion:** Young adults presented with repeated attacks of peripheral nerve palsies with no obvious clinical explanation warrant further evaluation for this rare condition. Early suspicion of this entity and correct diagnosis enable early counselling and management including avoidance of repeated cycles of unnecessary investigations during recurrent disease attacks.

## Pyogenic Meningitis in Patients with a History of Irradiation for Nasopharyngeal Carcinoma

Choi-ting Tse, Koon-ho Chan, Raymond Tak-fai Cheung  
Queen Mary Hospital, Hong Kong SAR

**Background:** Nasopharyngeal carcinoma (NPC) is a common cancer in the Southeast Asian territory. When patients with a history of NPC develop pyogenic meningitis, the overall mortality rate has been reported to be higher than those without NPC. Similar data from Hong Kong are lacking.

**Methods:** Medical records of a total of 26 cases of pyogenic meningitis admitted to neurology ward, Queen Mary Hospital, from January 1997 to June 2008 were reviewed. The Glasgow Coma Scale (GCS) at presentation, time delay between admission and initiation of antibiotics, duration of hospital stay, Barthel Index (BI) upon discharge and immediate outcome were reviewed.

**Results:** Mean age of the study cohort was 52.2 years, and the male-to-female ratio was 1.2:1. Five of the 26 cases had a history of NPC with irradiation prior to development of meningitis. The mean time lag between diagnosis of NPC to development of meningitis was 8 years (range, 1-23 years). There was no significant difference in GCS at presentation (15/15 in NPC group vs 13.8/15 in non-NPC group). Although there was a difference in time delay between admission and initiation of antibiotics (60.2 hours in NPC group vs 12.9 hours in non-NPC group), there was no difference in BI upon discharge (80/100 in NPC group vs 85.8/100 in non-NPC group) as well as in the duration of hospital stay (21.8 days in both groups). Mortality rate was 20% in NPC group (1/5) and 9.5% in non-NPC group (2/21).

**Conclusion:** A history of NPC with irradiation does not seem to be a poor prognostic factor for patients with pyogenic meningitis. Outcome following rehabilitation is comparable between the two groups of survivors, irrespective of the history of irradiated NPC.

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**Background:** A multi-disciplinary home mechanical ventilation (HMV) service for patients with chronic respiratory failure due to neuromuscular disease was established since April 2007. The programme provided (a) comprehensive clinical assessment to indicate the suitability of HMV, (b) “priming” service for patients with foreseeable risk of developing respiratory failure, and (c) follow-up to all patients put on home ventilatory support. The programme aims to provide quality HMV service, reduce unplanned hospitalisations, avoid emergency intubations, and improve quality of life of these patients. A pilot study was conducted to examine the short-term outcomes of the programme and to explore potential areas for further improvement.

**Methods:** The following data were collected prospectively: (1) epidemiological data, (2) underlying neuromuscular disease and co-morbidities, (3) subsequent need of emergency resuscitation and intubation, (4) subsequent unplanned readmissions, and (5) subsequent unplanned readmissions. These outcome parameters were collected and recorded in a follow-up programme after setup of HMV.

**Results:** Thirteen patients with neuromuscular diseases were assessed in November 2007. Nine patients were put on home ventilatory support. One patient with motor neuron disease refused HMV despite full explanation and died subsequently from respiratory failure. The remaining three patients were actively monitored for evidence of developing overt respiratory failure. Among the nine HMV patients, six were ventilated before commencement of programme (the pre-HMV group). All underwent emergency intubations and all were invasively ventilated via tracheostomy. Their mean age was  $55.5 \pm 22.8$  years and their mean hospital stay was  $219 \pm 120$  days. The three patients enrolled after April 2007 (the post-HMV group) were all ventilated non-invasively via face mask. Their mean age was  $53.7 \pm 4.73$  years and their mean hospital stay was  $18.3 \pm 4.51$  days. There were three unplanned readmissions in both the pre-HMV group and post-HMV group. All were related to pneumonia. The mean length of hospitalisation in the pre- and post-HMV group was  $13.3 \pm 7.7$  days and  $4.4 \pm 2.5$  days respectively ( $P=0.298$ ).

**Discussion:** This was considerable demand for home ventilation service for patients with neuromuscular diseases. A multi-disciplinary priming service (including end-of-life support) was offered before HMV commencement to enhance acceptance and preparation for subsequent need of HMV. For those patients who refused HMV, the service could avoid unnecessary resuscitations, prolongation of sufferings, and potential conflicts between relatives and hospital staff. For those who opted for HMV, non-invasive ventilation (NIV) could be tried initially to avoid psychological stress related to the need of tracheostomy and to reduce risk of subsequent chest infection. The duration of hospitalisation was much shorter for NIV titration when compared to invasive ventilation. Close monitoring was provided to those patients with impending respiratory failure and those being put on non-invasive ventilatory support. Pneumonia accounted for most of the unplanned hospitalisations. The frequency of unplanned readmissions did not change but a trend towards shorter hospital stay was observed.

**Conclusion:** A systematic and multi-disciplinary programme before commencement of HMV in neuromuscular disease patients with impending respiratory failure might provide better acceptance, reduce emergency intubations and rate of tracheostomies, as well as shortening the length of hospitalisation.

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**Background:** To review the trend of incidence of intracerebral haemorrhage, their mortality and morbidity rate and factors affecting outcome.

**Methods:** Retrospective study on a prospectively collected cohort in a regional hospital in Hong Kong.

**Results:** A total of 4073 patients were available for analysis; 558 of these have their first stroke as intracerebral haemorrhage. The percentage with intracerebral haemorrhage as first stroke reduced from 24.5% in 1996-97 to 16.2% in 2002-03. The overall mortality rate was 33.2%. The 30-day mortality reduced from 42 to 37.6% at 30 days, while the 1-year mortality reduced from 47 to 29% until the final year which rose to 44.6%. The factors predicting mortality at 30 day included NIHSS >20, age >70, and the result reached statistical significance. The presence of hypertension and hypercholesterolaemia predicted survival at 30 days. We observed that the trend of intracerebral haemorrhage as first-ever stroke was decreasing. This could be due to better blood pressure control with newer anti-hypertensive agents, a better recognition of stroke, more conscious stroke prevention, and better quality of stroke care. On the contrary, this could represent an increased proportion of ischaemic stroke due to a shift to a more western diet leading to increased prevalence of atherosclerotic diseases.

**Conclusion:** The percentage of patients with first-ever stroke as intracerebral haemorrhage is reducing over the 10 years. The 30-day mortality is improving while the 1-year and 5-year mortality did not show a similar trend. An NIHSS score >20 and age >70 predicts mortality at 30 days, while the presence of hypertension and hyperlipidaemia at presentation predicts survival at 30 days.

# Genetic Diagnosis of Hereditary Spastic Paraplegia

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**Background:** Hereditary spastic paraplegias (HSP) are a clinically and genetically diverse group of chronic central motor system disorders, characterised by progressive lower limbs spasticity. This disorder is clinically classified into pure and complicated forms. At least 38 genetic loci are associated with HSP; HSP can be inherited as autosomal dominant, recessive and X-linked. Genotype data in Hong Kong remain unknown. We report the mutational studies of three unrelated HSP families.

**Methods:** Case 1 presented with spastic paraplegia since 3 years old. His father and elder sister were also affected at similar age. Case 2 suffered from lower limb weakness and spasticity since 30 years old and was wheelchair bound at present. Several family members had similar problems. Case 3 presented with repeated falls since 17 years old and progressed to spastic paraplegia. The first two cases were Hong Kong Chinese. The third case was a Pakistani with consanguineous parents. There were no other neurological deficits and the NCV was normal. MRI brain of case 3 revealed an isolated corpus callosum atrophy. Molecular analyses of SPG3A on case 1, SPAST (SPG4) on case 2 and SPG11 on case 3 were performed using PCR and direct DNA sequencing.

**Results:** Heterozygous mutation of p.R239C on SPG3A and p.P361L on SPAST was found in case 1 and case 2 respectively. Case 3 carried a homozygous nonsense mutation p.W89X on SPG11. All were known disease-causing mutations.

**Conclusion:** Detailed clinical and family history with neurological investigations is important for prioritising molecular testing. Mutations in SPAST are responsible for approximately 40% of autosomal dominant pure HSP and SPG3A approximately 10%. SPG11 accounts for approximately 50% of autosomal recessive complicated HSP. The identification of mutation is important in providing prognosis, genetic counselling and estimation of recurrence risk in family members. We report the first mutational confirmation of HSP on SPG3A, SPAST, and SPG11 in our locality.

## Incidence of Significant Extracranial Carotid Stenosis in Acute Ischaemic Stroke

FP 11

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**Background:** Atherosclerotic carotid disease is a significant cause of ischaemic stroke. Local data are limited.

**Methods:** Retrospective review of early carotid doppler ultrasonography (USG) scanning result in acute ischaemic stroke patients.

**Results:** Data were extracted from our hospital stroke database and vascular laboratory database between 1 January 2006 and 31 December 2006. There were 915 stroke and 102 transient ischaemic attack (TIA) admission in year 2006, 772 cases were ischaemic stroke, male-to-female ratio was 0.96, mean age was 73. Carotid doppler USG was performed in 391 ischaemic stroke and 46 (43%) TIA patients before hospital discharge. A total of 273 Doppler USG were performed in vascular laboratory, 52 scanning were performed in Department of Radiology, 125 were performed in EDU of Department of Medicine. We analysed the data from vascular laboratory. Of 273 cases, 32 showed more than 50% stenosis of ICA (12 cases of 50-69%, 10 cases of 70-99%, 10 cases of total occlusion), seven cases had bilateral >50% stenosis. Six cases had non-symptomatic side stenosis. Three cases refused intervention. Three cases had no further workup due to medical reason (1 had poor stroke recovery, 1 had concomitant illness, 1 died within 30 days). Twenty cases had followed MRA or CTA performed for confirmation, 17 cases showed good correlation with USG-defined stenosis severity, one case showed slight over-estimation by USG (from 80-99% by USG to 75% by CTA). Two cases showed major overestimation with alteration of management decision (both cases from 50-69% down to about 40%).

**Conclusion:** There was a huge workload of carotid Doppler USG for acute ischaemic stroke patient. A significant proportion of ischaemic stroke patient had high degree of carotid stenosis. There is good correlation of Doppler USG finding with MRA or CTA. More resource is needed to provide early carotid USG screening for acute ischaemic stroke patients.

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**Background:** Dopa-responsive dystonia (DRD) is a clinical diagnosis characterised by dystonia, parkinsonism, diurnal worsening and a dramatic therapeutic response to L-dopa. However, presentations can be protean and therapeutic response is not uniformly successful. Dopa-responsive dystonia comprises a heterogeneous group of disorders affecting the synthesis of cerebrospinal fluid (CSF) neurotransmitters leading to dopamine deficiency. This group includes at least the autosomal dominant and recessive forms of GTP cyclohydrolase 1, tyrosine hydroxylase deficiency and juvenile onset Parkinson's disease. A simple clinical diagnosis of DRD is not sufficient. Genotype data in Chinese are largely unknown. We report the biochemical and mutational characteristics of 16 unrelated Chinese families with DRD.

**Methods:** Molecular analyses of GCH1, TH, and/or PARK2 genes were performed on 16 unrelated Chinese DRD patients by polymerase chain reaction, DNA sequencing and multiplex ligation-dependent probe amplification. Cerebrospinal fluid neurotransmitters and pterins were determined by high-performance liquid chromatography.

**Results:** The majority were tyrosine hydroxylase deficiency (53.3%). Four were autosomal dominant GTP cyclohydrolase 1 deficiency and three were juvenile onset Parkinson's disease. We characterised 22 different mutations with 14 novel mutations. The novel mutations were p.A98T, and p.Q182E, and p.Met211ValfsX38 in GCH1; p.R153X, p.G216S, p.Q232X, p.P249L, p.G263R, p.G284S, p.I363T, p.A354V, p.G377R, and c.1163+5G>C in TH and c.1378dupG in PARK2. The clinical phenotypes cannot predict genetic pathogenesis. The typical pattern of CSF neurotransmitters in tyrosine hydroxylase deficiency was only observed in one patient. Others showed inconsistent patterns.

**Conclusion:** Our study confirmed the heterogeneous pathogenesis of DRD in Hong Kong Chinese. A clinical diagnosis is simply inadequate. The diagnosis of DRD should be confirmed by mutational analysis. A precise genetic diagnosis is crucial for proper genetic counselling, optimal treatment, estimation of potential recurrence risks for family members as well as prenatal diagnosis.

## DNA-based Diagnosis of Severe Myoclonic Epilepsy of Infancy (Dravet Syndrome) in Hong Kong Chinese

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**Background:** Mutations in genes encoding ion channels in brain neurons have been identified in various epilepsy syndromes. Severe myoclonic epilepsy of infancy (SMEI) affecting the voltage-gated sodium channel alpha subunit was first described by Dravet in 1978. SMEI is a catastrophic infantile-onset epilepsy. Affected infants develop multiple seizure types such as generalised tonic-clonic (GTC), focal, absence and myoclonus. Seizures are often fever-sensitive. Psychomotor retardation, recurrent status epilepticus and other neurologic deficits can occur. EEG findings are not definitive. Genetic diagnosis is important for the choices of anti-epileptic drugs and genetic counselling.

**Methods:** Case 1 presented with recurrent febrile seizures since 6 months old. She had a history of status epilepticus requiring ICU care at 15 months. She developed multiple seizure types (GTC, focal and absence seizures) which were aggravated by tegretol but well-controlled by epilim and clobazam. She had mild ataxia. Case 2 and 3 also presented with recurrent febrile seizures since infancy and suffered from intractable seizures with multiple types. Case 2 had progressive mental regression. MRI brain was normal. Molecular analysis of all the coding exons and their flanking introns of SCN1A was performed by PCR and direct DNA sequencing.

**Results:** Cases 1, 2 and 3 were heterozygous for p.Q450X, p.V1601I and p.L1318P respectively. All were novel mutations. p.Q450X causes a premature stop codon and conceivably leads to defective voltage-gated sodium channel. The latter two mutations were not found in 100 normal chromosomes and the involved amino acids were strictly conserved in evolution analysis.

**Conclusion:** A new paradigm of channelopathy in epilepsy syndromes is excitingly evolving into the understanding of epilepsy pathogenesis. SMEI is one example. DNA-based diagnosis enables accurate and early diagnosis for optimal management plan. We report the mutational findings of the first case series of SMEI in Hong Kong Chinese.

## Prognostic Value of Motor Evoked Potential Obtained by Transcranial Magnetic Stimulation in Motor Recovery in Patients with Acute Ischaemic Stroke in Kwong Wah Hospital

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**Objectives:** To investigate whether motor evoked potential (MEP) correlates with motor performance and whether MEP is an independent prognostic indicator of motor outcomes in acute ischaemic stroke.

**Design:** This was a prospective study using single-pulse transcranial magnetic stimulation (TMS) for investigating the functional role of the corticospinal tract in a group of patients with limb weakness caused by acute ischaemic stroke. Patients were being followed up to 6 months after acute stroke event.

**Setting:** Acute Stroke Unit, Kwong Wah Hospital.

**Subjects and Methods:** Fifty-three consecutive stroke patients fulfilling the inclusion criteria were included in this study. Transcranial magnetic stimulation was used to determine the presence or absence of MEP and stroke outcome was assessed up to 6 months.

**Outcome measures:** Main outcome measure with upper limb motor recovery was assessed by handgrip power at 0th month, 3rd month, and 6th month. Secondary outcome measures included Box and Block Tests, 9 Hole Peg Test, Frenchay Arm Test and Barthel Index.

**Results:** Motor evoked potential correlated with handgrip power at initial and 3rd-month post stroke. No statistical significant result was found in primary outcome measure with change of handgrip power as well as secondary outcome measures including change of Box and Block Test, 9 Hole Peg Test and Barthel Index in MEP-present versus MEP-absent group.

**Conclusion:** Motor evoked potential correlates with handgrip power at initial and 3rd-month post stroke. Preservation of MEP alone is not a useful parameter for prediction of motor recovery.



## The Prevalence of Depression and Cognitive Impairment in Chinese Parkinson's Disease Patients

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**Background:** For historical background, Parkinson's disease (PD) has been well recognised as a neurodegenerative disease, which mainly presents with motor symptoms. Until recently, it has been found that non-motor symptoms (NMS) of the disease are of at least equal importance in the management of patients with PD. The prevalence and pathophysiology of the non-motor aspects of PD were extensively studied in other countries. Knowledge about local prevalence of such symptoms among our PD patients is necessary in order to allow early recognition of them and appropriate management.

**Objective:** To study the prevalence of cognitive impairment and depression among PD patients in a regional hospital in Hong Kong.

**Method:** This was a prospective questionnaire survey to determine the prevalence of depression and cognitive impairment among our PD patients. During the predefined study period (Oct 07 to Mar 08), all eligible PD patients visiting the Movement Clinic of the United Christian Hospital were recruited. All patients who met the idiopathic PD diagnostic criteria of UK PDS and were able to give the consent were included. A short interview was conducted. Five different screening questionnaires were used including Geriatric Depression Scale-15 (GDS-15), Hamilton Depression Rating Scale-17 (HDRS-17), Mini-Mental State Examination (MMSE), Frontal Assessment Battery (FAB), and Non-Motor Symptoms Questionnaire (NMS Quest) of PD.

**Results:** One hundred and eleven patients completed the interviews and questionnaires. The mean age was 67 (SD, 9) years and 68.5% were male patients. The duration of illness was  $6.5 \pm 5$  years. Summation of the UPDRS II & III was  $26.6 \pm 15.3$  and modified Hoehn and Yahr Score was 2.5 (IQR, 1-2.5). The prevalence of depression screened by HDRS-17 ( $\geq 10$ ) was 25.2% while screened by GDS-15 ( $\geq 8$ ) was 43.2% in Chinese PD patients. The prevalence of dementia screened by MMSE ( $\leq 22$  in educated and  $\leq 18$  in non-educated) was 11.7% and that of the frontal lobe dysfunction screened by FAB ( $\leq 12$ ) was 47.7%. The mean NMS score was  $8.5 \pm 5$ . There was apparent association of the total NMS scores across different stages of the motor severity. Depression, frontal lobe dysfunction, dementia and other NMS were significantly correlated with the motor severity of PD.

**Conclusion:** Depression and cognitive impairment in addition to NMS are highly prevalent in Chinese PD patients. In order to improve the quality of life in our patients, early recognition of these symptoms is essential.

## The Occurrence Rate of Excessive Daytime Sleepiness in Local Parkinson's Disease Patients and Its Disease-specific Risk Factors

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**Background:** We usually focus on the motor symptoms and the complications of Parkinson's disease (PD) but the non-motor problems like excessive daytime sleepiness were often ignored by both the patients and doctors. In fact, it is common and affects their quality of life and prone them to accidents. However, the local data concerning about excessive daytime sleepiness and its predictive factors were lacking. There was no clear consensus about the predictive factors from many previous studies. Besides, the results were slightly different from the studies between Caucasian and Asian populations. Therefore, we can provide better patient care management when the predictive factors were understood fully.

**Objective:** To study the occurrence rate of excessive daytime sleepiness by Epworth sleepiness scale (ESS) in our local PD patients compared with age- and sex-matched non-PD controls and to find out its predictive factors for excessive daytime sleepiness among the PD patients.

**Methods:** The 3-month study was performed in the neuromedical out-patient clinic of Kwong Wah Hospital. It comprised 99 PD patients and 103 age- and sex-matched controls. Epworth sleepiness scale was employed to screen for excessive daytime sleepiness in the structured questionnaire during the interview. The univariate and multivariate analyses were used to find out the association between variables and excessive daytime sleepiness.

**Results:** The mean ESS of PD patients was  $9.89 \pm 3.73$  versus  $4.69 \pm 3.27$  ( $P=0.000$ ) in age- and sex-matched controls. There were 56.6% of PD patients with ESS more than or equal to 10 compared with 11.7% of the controls ( $P=0.000$ ). There were nine variables including age, PD duration, PD severity, levodopa dose, sleep quality score, sleep time, sleep latency, number of awakening per night, and PD sleepiness scale showed a significant correlation with excessive daytime sleepiness. The multivariate logistic regression analyses revealed that PD severity, levodopa dose, sleep quality score and number of awakening per night were found to be the disease-specific risk factors for excessive daytime sleepiness among the PD patients.

**Conclusion:** The occurrence rate of excessive daytime sleepiness in PD is 56.6% that was shown to be really a common problem in our local PD patients. The PD severity, the levodopa dose, sleep quality score and number of awakening per night were specific predictor factors. Therefore, the excessive daytime sleepiness is multi-factorial and related to the disease pathology itself, medication and sleep problem.

## The Updates of Managing Cervical Dystonia/Movement Disorders with Botulinum Toxin

S 1

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Botulinum toxin is a neurotoxin protein produced by the bacterium *Clostridium botulinum*. Being one of the most poisonous naturally occurring substances and the most toxic protein, it has become one of the most widely used and most effective therapeutic agents ever invented. Botulinum toxin type A was first used in human strabismus in 1980. In less than three decades, its applications have expanded greatly. Nowadays it is used to treat all kinds of dystonic or non-dystonic muscle spasm, sphincter problems, headache, excessive sweating or salivation, spasticity of all sorts, and facial wrinkles. Dystonia has been the first movement disorder treated with botulinum toxin. However, the use of botulinum toxin has encompassed many other hyperkinetic movement disorders, such as tremor, tics, tardive dyskinesias, and bruxism. This tremendous explosion in the use of botulinum toxin is attributed to its effectiveness and relative lack of severe side-effects. For this agent, the discovery of new and novel uses is limited only by our own creativity. During clinical practice, it is advisable to keep some points in mind before commencing botulinum toxin treatment. The principal symptom being targeted should be clear. For example, is botulinum toxin given to relieve pain, or to correct abnormal posture, or both? Muscles that are principally causing the symptom(s) are then identified. A sufficient dose should be injected into each muscle. The main goal of botulinum toxin injection is to maximise benefit and to limit potential side-effects. For each treatment, we should review with the patient on our expectations on the expected treatment effect. Despite its proven therapeutic value, there are still many unresolved issues and concerns about botulinum toxin. For example, there is still no standardisation of biological activity of the different preparations, and the understanding of toxin antigenicity is poor. Clinicians interested in using botulinum toxin chemodenervation in their practice must be aware of these concerns and should exercise proper precautions to minimise the potential risks associated with the toxin.

## Basal Ganglia Motor Dysfunctions: a Basic Scientist's Perspective

S 2

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Looking back on the scientific and clinical researches done on basal ganglia motor dysfunctions over the last two decades, there is no doubt that very significant advances have been achieved. The evolutionary idea on distinct signalling channels with the basal ganglia, namely the 'direct' and 'indirect' pathways model, has led to the invention of innovative approaches such as deep brain stimulation (DBS) in treating certain groups of Parkinson's disease patients. The extensive application of DBS in the last decade proved that it is useful not only in treating Parkinson's disease but also beneficial in some other neurological and psychiatric disorders. However, despite such advances, there are still many aspects and questions about the basal ganglia, especially from the point of view of basic science, that have not been solved. The answers to these questions will likely have large impacts not only in understanding the functions of the basal ganglia but also the treatment of their diseases. A few of these questions, which reflect my personal interest and bias in the subject, include the following.

One fundamental question concerns why and how dopamine neurons die in the substantia nigra pars compacta in Parkinson's disease. While the answer to this question remains mysterious, some interesting hypotheses have been put forward in recent years to explain the selective vulnerability of these neurons, for example, the calcium channel hypothesis. Second, our knowledge about the basal ganglia circuitry under normal and parkinsonian states has expanded much in recent years. Combining with the newly described adaptational changes found in different basal ganglia nuclei, including the striatum, globus pallidus and subthalamic nucleus, necessitates the reappraisal of the well-accepted basal ganglia model. Finally, despite its remarkable effectiveness, what the mechanism of DBS is and why it is effective are still largely unknown. Although it is clear that the clinical development of DBS did not require a full understanding of its mechanism, such knowledge can provide the rationale for adopting DBS in new clinical application. Some of the proposed physiological actions of DBS will be discussed.

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Neuromyelitis optica (NMO) is the first inflammatory autoimmune demyelinating disease of the central nervous system (CNS) for which a specific tissue target molecule has been identified—the astrocytic water channel aquaporin-4 (AQP4). Immunological insights have propelled significant advances in understanding the clinical, radiologic and immunopathologic characteristics of the disease in the last 4 years.<sup>1-6</sup> Ethnicity is an important but poorly understood determinant of susceptibility to and phenotype/severity of this disorder. Neurological signs of AQP4 autoimmunity in children extend beyond the optic nerve and spinal cord more frequently than in adults. This presumably reflects differences in adult and juvenile CNS maturation and AQP4 distribution. Development of effective, and potentially curative, therapies requires validated models of the disease, in animals and cell culture systems. NMO-IgG is a clinically validated serum biomarker that distinguishes relapsing CNS inflammatory demyelinating disorders related to NMO from multiple sclerosis (MS). The NMO-IgG autoantibody targets astrocytic aquaporin-4 (AQP4) water channels. Clinical, radiological and immunopathological data support a primary role for NMO-IgG in the pathogenesis of NMO-spectrum disorders. Characteristic CNS lesions are distinct from MS by exhibiting selective depletion of AQP4 and the major glutamate transporter of the CNS, EAAT2,<sup>4,7</sup> with and without associated myelin loss, focal vasculocentric deposits of IgG, IgM and complement, prominent oedema and inflammation.<sup>4</sup> NMO-IgG targets astrocytes directly. In the presence of active complement, astrocyte membrane integrity and blood-brain barrier permeability are compromised, and granulocytes are attracted to the site of complement activation.<sup>7,8</sup> In the absence of complement, astrocytic membranes remain intact but AQP4 is endocytosed with concomitant loss of Na<sup>+</sup>-dependent glutamate transport and loss of the EAAT2 transporter.<sup>7</sup> IgG binding to AQP4, in the absence of complement, additionally targets astrocytes for antibody-dependent cell-mediated cytotoxicity.<sup>8</sup> Thus, binding of NMO-IgG to astrocytic AQP4 initiates several potentially neuropathogenic mechanisms: complement activation, AQP4 and EAAT2 down-regulation with disruption of water and glutamate homeostasis, enhanced blood-brain barrier permeability, IgM and granulocyte influx, and antibody-dependent cell-mediated cytotoxicity.

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Stroke is not an accident but a brain attack. It ranks second among the world's leading causes of death. Among all adult neurological diseases, stroke ranks number one in frequency and importance. Ischaemic stroke accounts for about 80% of all strokes and haemorrhagic strokes for about 20%. Annually more than six million people die of stroke in the world. In addition, stroke survivors outnumber stroke deaths by three folds, and persistent neurological disability of varying degrees is common among stroke survivors.

An unstable ischaemic penumbra allows acute therapy for ischaemic stroke and thus stroke is a true neurological emergency. Time window for intravenous thrombolysis has recently been extended to 4.5 hours after onset, and endovascular thrombolysis or thrombectomy has a time window of 6 hours. Managing stroke patients in a stroke unit will improve outcome and reduce mortality.

The 'time is brain' concept demands acute stroke care and avoidance of delays. Pre-hospital delay should be tackled via public education on recognising stroke symptoms and appropriate attitudes to acute stroke as well as use of emergency ambulance service. In-hospital delay is due to a failure to identify stroke as an emergency, inefficient in-hospital transport, delayed medical assessment, delay in imaging and uncertainty in administering thrombolysis.

There is much room for improvement of acute stroke care in Hong Kong. In the Hong Kong West Cluster, neurologists, neurosurgeons, radiologists, emergency physicians, rehabilitation specialists, nurses and administrators have worked together to organise an acute stroke care pathway. The pathway will run 24 hours a day and for 7 days a week and involve rapid triage of patients presenting with stroke or transient ischaemic attack at the Emergency Department, immediate neuroimaging, direct admission to a comprehensive acute stroke centre with intensive monitoring, joint management by neurologists and neurosurgeons, protocol-driven administration of thrombolysis, consideration of endovascular or neurosurgical interventions, subsequent management in designated stroke beds and early commencement of rehabilitation.

## A Novel Treatment Modality for Intracerebral Aneurysm

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Microsurgical and endovascular techniques for cerebral aneurysm treatment have improved over the last few decades. However, very wide-necked and fusiform aneurysms provide considerable difficulties to neurosurgeons because they are not amenable to conventional coil embolisation or surgical clipping. The Pipeline embolisation device (PED) is a new endovascular construct designed to exclude aneurysms from the parent cerebrovasculature. The device consists of a braided mesh cylinder composed of individual platinum and cobalt chromium microfilaments. When fully deployed, the implants are designed to provide approximately 30 to 35% metal surface coverage at nominal expansion, which is a much higher percentage of coverage than that provided by conventional (non-covered) intravascular stents. A review of the concept of flow diversion by using stenting alone is presented, followed by a report of a small case series of using this device in Hong Kong.

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The imaging of epileptic patients serve two purposes: firstly, to identify underlying structural abnormalities that require specific treatment (such as surgery) and secondly, to aid in formulating a syndromic or aetiological diagnosis.<sup>1,2</sup> Refractory epilepsy occurs in at least 30% of epileptic patients and surgical management has an increased importance in this group of patients. This talk is an overview of the role of modern neuroimaging in identifying structural and functional abnormalities in patients with refractory epilepsy.

The commonest forms of paediatric refractory epilepsy presenting to surgery include malformation of cortical development (with various forms including hemimegalencephaly, tuberous sclerosis complex and developmental tumours), hippocampal sclerosis, cavernous malformations etc.<sup>3</sup> Classic examples and cases would be discussed during the talk.

High-quality neuroimaging is indispensable for evaluating the type, anatomical location and extent of the morphological structural lesion. High-field magnetic resonance imaging (MRI) is the preferred modality because of its excellent spatial resolution, soft tissue contrast and multi-planar capabilities.<sup>1</sup> The functional deficits possibly related to the epilepsy can be evaluated by functional imaging techniques such as ictal SPECT, interictal PET and functional MRI.<sup>4</sup> The first part of the talk is on structural MRI and second part on application of functional imaging techniques.

The primary aims of the pre-surgical evaluation are to collect the information relevant to the localisation of the epileptogenic zone and the estimation of a possible post-surgical deficit. These include MRI, ictal surface EEG, semiology, PET (or SPECT) and psychological assessment.<sup>4</sup> The future role of sophisticated functional neuroimaging techniques such as fMRI, diffusion tensor imaging (DTI), neuro-PET techniques will be briefly discussed.

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Cerebrovascular disease is one of the major causes for mortality and hospital admission in our locality. The proper management of these patients is therefore very important, both medically, economically and socially.

To make the diagnosis of haemorrhagic stroke can be easily done by a rapid computed tomography (CT) imaging. With the current technology, the scanning time is less than 1 minute. With a major change in the management of ischaemic stroke in recent years, the therapeutic window for intra-arterial and intravenous thrombolysis remains narrow, a prompt and accurate diagnosis is therefore important.

Popularity of higher field scanners means an increase in signal-to-noise ratio, by which small lesions can now be clearly depicted. Small and distal vessels can now be better assessed by magnetic resonance angiography. Another advantage of the higher field scanners is the shortened scanning time, of which the image quality can be improved in confused and un-cooperative patients. Relatively long sequences such as diffusion tensor tractography might become part of the routine clinical assessment in the future.

Plaque imaging of extracranial and intracranial vessels is now technically feasible, enabling better understanding of the pathophysiology of cerebrovascular disease. With shortened imaging time and scanning cost, plaque imaging might have a potential role in monitoring of response to therapy.

There are parallel advances in CT. Computed tomography has now evolved from single-detector CT to multidetector CT, which means a significant improvement in spatial and temporal resolution. With a 64-detector CT, up to 4 cm of brain parenchyma can now be covered in the perfusion scans. Even newer CT scanners allow coverage of the whole brain in a dynamic sequence, CT brain perfusion might represent an attractive alternative for patients with contra-indications to magnetic resonance imaging (MRI). With the new CT scanners, contrast CT angiography covering the whole neck and the brain can be performed with smaller dose of iodinated contrast, allowing CT brain perfusion and CT angiography to be performed under the same setting. This would potentially allow expansion of the role of CT in diagnosing acute stroke in the A&E department.

Besides CT and MRI, there are also wider applications of ultrasound. Cerebral blood flow measurement can now be achieved by Doppler imaging, which can be performed in the bedside and is relatively cheap. It definitely has its advantages over CT and MRI in patients with allergy history or renal impairment. It is also ideal for serial follow-up for monitoring the response to therapy, as no radiation is involved and contrast is not required.

In summary, advances in imaging technology have allowed better and faster diagnosis of cerebrovascular disease. It has also widened the role of imaging in stratification of patients, selection of suitable treatment method for individual patients and monitoring of the response to therapy.

**Eric Leung**

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The population aged 65 and above in Hong Kong in mid 2007 was 12.6%. It is expected to increase to 20% in the next 10 years. Dementia, being an age-related disease, is expected to increase. In Hong Kong, 4% of elderly persons aged 65 or above and 6% of those aged 70 or above suffer from dementia. The current number of dementia cases is estimated to be approximately 60 000. It is estimated that if one can delay the onset of dementia by 5 years, the prevalence of the disease would be decreased by 50%.

The most common form of dementia among older people is Alzheimer's disease (AD). Other causes of dementia includes parkinsonism dementia, vascular dementia, Lewy body diseases, frontotemporal dementias, depression, Down's syndrome, endocrine disease, hydrocephalus, tumour, infection, overmedication, and toxic conditions.

Alzheimer's disease is named after Dr Alois Alzheimer, a German doctor. In 1906, Dr Alzheimer noticed changes in the brain tissue of a woman who had died of an unusual mental illness. He found abnormal clumps (now called amyloid plaques) and tangled bundles of fibres (now called neurofibrillary tangles). Today, these plaques and tangles in the brain are considered neuropathological hallmarks of AD.

Patients who suspected to have AD should be screened by clinical history, proper physical examination, psychometric testing, baseline laboratory, and radiological investigation for treatable causes. There is usually no difficulty in differentiating normal and established AD patients. Most of the current treatment for AD is to prevent the progression or deterioration of disease. If we can diagnose the disease in early stage, there will be a good chance that patient will not progress into clinical AD. The goal of delaying this disease for 5 years seems not unreachable.

The real situation is that it is sometimes difficult to differentiate amnesia with normal ageing from mild cognitive impairment (MCI). Mild cognitive impairment is different from both AD and normal age-related memory change. People with MCI have ongoing memory problems, but they do not have other losses such as confusion, attention problems, and difficulty with language.

Magnetic resonance imaging (MRI) and positron emission tomography (PET) scans, or other imaging or biological markers, can see early AD changes or measure disease progression.

In normal subjects, regional glucose metabolism and blood flow are tightly coupled to the neuronal function. In neurodegenerative disease, both are reduced due to regional synaptic dysfunction. <sup>18</sup>FDG PET brain scan has long been used as a functional assessment of regional brain metabolism. This serves to assess the severity and chronicity of disease. The classical distribution of metabolism with hypometabolism in bilateral temporal and parietal lobes can also help to differentiate AD from vascular dementia, frontotemporal dementia, Huntington's disease, Parkinson's dementia, and dementia with Lewy bodies (DLB). There is about 85-95% sensitivity and 70-90% specificity. The accuracy is influenced by age and disease severity. This is more useful in patients with established AD (ie there is already synaptic damage) for the assessment of disease severity and treatment response. Patients with preclinical stage of AD or MCI may show impairment of glucose metabolism in posterior cingulate gyrus and precuneus or remain normal.

If a pre-symptomatic scan was found to predict a favourable response to a disease-modifying treatment, then screening scan might be used to identify candidates for treatments that would hold brain protein deposits at brain, in order to delay the onset of AD. Recently, various PET ligands used in amyloid imaging have been developed. With over 700 amyloid brain scans research being reported worldwide, consistent results show that amyloid PET brain scan is able to assess the amyloid load in the brain. That is to diagnose those patients with amyloid laden pathology or to predict those patients at high risk of progression to AD.

Promising results have been obtained with N-methyl <sup>11</sup>C 2-(4'methylaminophenyl)-6-hydroxy-benzothiazole (PIB). This PIB binds with high affinity and high specificity to neuritic amyloid beta plaques. There is no significant binding to diffuse plaques, neurofibrillary tangles or pure Lewy body brain homogenates. It was found to discriminate successfully between AD patients and age-matched healthy control. Longitudinal studies also showed PIB could differentiate MCI converter to AD from MCI non-converter. Research data suggest that amyloid beta deposition is an early event and likely to occur prior to demonstrable cognitive impairment. Patients with MCI with high PIB retention in the frontal, parietal and temporal cortices as well as the posterior cingulate gyrus and precuneus were more likely to progress



to AD. The fact that PIB uptake usually peaks at the early stage of AD makes it difficult to assess disease severity. This drawback can be overcome with FDG PET scan which can assess reduction of cerebral glucose metabolism relating to disease severity.

It has been reported that up to 15% of healthy ageing population with normal cognitive function show mild PIB uptake significantly less than that of AD patients. We do not know whether this group of normal population is 'true normal' or they will progress to AD in a longer time frame. There is postmortem evidence that amyloid plaques deposition may begin up to 10 years before the onset of AD. This needs further extensive research to validate. If the latter is true and if the passive immunisation is found to be safe and effective, PIB scan can serve as a surrogate measure of response to anti-amyloid therapy. It is expected that the incident of dementia would drop substantially in the future.

Parkinsonian disorder, being an age-related disease, has high incidence in elderly patients (10 times more frequent after the age of 70). It includes mostly of Parkinson's disease (PD), DLB, atypical parkinsonisms-like progressive supranuclear palsy (PSP), multiple system atrophy (MSA) and corticobasal degeneration (CBD). Each disease entity has their unique clinical presentation. However it may be difficult to differentiate patients with atypical presentation on clinical assessment alone. According to clinico-pathological study, clinical diagnosis of PD was confirmed at autopsy in only 76% of cases and 45% in MSA.

Neuroimaging utilising MRI, SPECT and PET examinations would be helpful in establishing the diagnosis. Nuclear medicine uses different tracers, specific for the dopamine transporting system or dopamine receptor ligands, which makes it possible to differentiate pre-synaptic dopaminergic system involvement from pre- and post-synaptic involvement.

Functional neuroimaging may be helpful in the assessment of the preclinical period of PD with potential early therapy (especially to those with high risk), the rate of progress (evaluation of the influence of drug treatment and stereotaxic surgery on disease progression) and the role of different structures in late complications. It also helps in the investigation of pathogenesis and pathology underlying the non-motor symptoms of PD and atypical parkinsonism as depression, dementia and psychosis.

Idiopathic PD is characterised by clinical symptoms of bradykinesia, rigidity, tremor, postural instability and good response to levodopa. Neuroimaging with visualising the dopamine synthesis ( $^{18}\text{F}$ -DOPA) and post-synaptic D2 receptors ( $^{11}\text{C}$ -raclopride) is helpful to study the nigrostriatal system. DOPA brain scan will show decrease uptake in contralateral putamen with normal-to-elevated raclopride uptake in early disease. With advanced disease, decrease DOPA uptake in contralateral caudate is noted, later with bilateral basal ganglia involvement. In MSA, CBD and DLB, decrease putamen DOPA uptake with impairment of raclopride D2 receptor uptake is expected. With PSP, the whole striatum show decrease DOPA uptake with preserved raclopride uptake. FDG brain scan is helpful to study regional brain metabolism. Each disease entity may show unique glucose metabolism. It is also useful to investigate non-motor symptoms associated with PD.

Shih-hui Lim

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Optimal management of patients with epilepsy requires accurate diagnosis of seizures and epilepsy syndrome. It is important to differentiate epileptic seizure (ES) from non-epileptic disorders, as well as epilepsy from reactive epileptic seizure disorders.

Epileptic seizure is a clinical event. Detailed specification of subjective and objective phenomena during epileptic seizure can be difficult. In addition, seizure presentation depends on location of seizure onset in the brain, patterns of propagation, maturity of brain, sleep-wake cycle and presence of medication.

According to the ILAE-IBE 2005's proposed definition of epileptic seizures and epilepsy, epileptic seizures are transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Without the electrical discharge criteria, many other clinical events that are not epileptic seizures might meet the other definition criteria. These disorders include vasovagal syncope, psychogenic seizures, movement disorders, cardiac arrhythmia, postural hypotension, migraine aura, sleep disorders, transient ischaemic attack, transient global amnesia, etc.

Definition of epilepsy is slight more controversial in the 2005's proposal. It is defined as a disorder of the brain characterised by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition. Previous definitions required presence of two or more unprovoked seizures. However newer proposal requires occurrence of at least one seizure, as long as the 'enduring predisposition' could be proven. Also the word 'unprovoked' has disappeared from the proposed definition.

Several cases will be presented to illustrate diagnostic challenges in the evaluation of patients with epileptic seizure and epilepsy.

## Treatment of Epilepsy in Patients with Comorbidities

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Seizures and epilepsy commonly occur in the setting of many general medical disorders. The seizure manifestations may have some characteristic features. The seizure occurrence may also have significant implications regarding the prognosis and treatment of the primary disorder, and the treatment of epilepsy and seizure may be influenced by the underlying comorbidities. Seizures are rare in hepatic encephalopathy. In general, the newer antiepileptic drugs (AED) undergo less hepatic metabolism and thus is less affected by hepatic diseases. As for the older AEDs, there is reduced protein binding of sodium valproate and phenytoin. However, clearance is usually unaltered, and toxicity from drug accumulation is unlikely unless the liver disease is severe. Hepatic encephalopathy may be precipitated by benzodiazepines, phenobarbital and other sedatives in patients with otherwise compensated liver disease. Seizure is said to occur in about one third of patients with acute renal failure and 10% of chronic renal failure. The seizures that occur in uraemia tend to be associated with a severe encephalopathy. Seizures may also occur during dialysis with disequilibrium syndrome. Myoclonic and non-convulsive status are not uncommon in renal impairment. In renal failure, protein binding, renal excretion and removal of drugs by dialysis may affect the AED use. In general, the newer AEDs are often excreted unchanged in the kidney. Dose adjustment is thus necessary in the presence of renal failure. As for the older AEDs, protein binding of phenytoin declines by up to 20%, resulting in lower therapeutic range of phenytoin in blood from 10-20 µg/mL to 5-10 µg/mL. 25% of phenobarbital is excreted unchanged in the urine. Accumulation of phenobarbital may occur in chronic renal failure, requiring lower maintenance dose.

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Hong Kong Epilepsy Society

At present, the delivery of epilepsy services in Hong Kong is heterogeneous and people with epilepsy may be under the care of general physicians, paediatricians, geriatricians, psychiatrists, neurosurgeons, neurologists, or epileptologists. A number of problems in relation to epilepsy care in Hong Kong are listed as follows:

1. Primary care: general practitioners are incompetent in management of epilepsy
2. Lack of referral channels, bridging service and structured teaching programmes
3. Epilepsy/Neurology clinics are flooded by patients with well-controlled epilepsy
4. Insufficient time and counselling are allocated to each patient
5. Scattering of resources
6. Absence of tertiary epilepsy centre and underdevelopment of epilepsy surgery

To improve the standard of care for people with epilepsy, our Society has formulated an evidence-based and practical clinical guideline on the modern management of epilepsy. The scope of the Hong Kong Epilepsy Guideline covers the following areas:

## Part I: The guideline

- Information given to people with epilepsy
- Following a first seizure
- Diagnosis, investigations and classification of epilepsy
- AED management of epilepsy
- Management of drug-resistant epilepsy
- Management of status epilepticus
- Perioperative management of seizure
- Referral for refractory epilepsy

## Part II: Special considerations

- Women with epilepsy
- Old people with epilepsy
- Children with epilepsy
- Lifestyle and other social issues

It is notable that a number of existing guidelines have been published by various professional and scientific organisations including:

1. NICE (UK) Guideline — more emphasis on cost-effectiveness <[www.nice.org.uk](http://www.nice.org.uk)>
2. SIGN Guideline <[www.sign.ac.uk](http://www.sign.ac.uk)>
3. ILAE publications <[www.ilae-epilepsy.org](http://www.ilae-epilepsy.org)>
4. Practice parameters of AAN <[www.aan.com](http://www.aan.com)>
5. Other regional guidelines, eg China, Malaysia, Italy

To avoid duplication of effort, both NICE and SIGN guidelines are used as framework during drafting of the Hong Kong epilepsy guideline. Updated evidence is generated via Medline search of original articles from 2003-2007 and using keywords, eg epilepsy, epileptic seizures, convulsions, neuroimaging, EEG and meta-analysis. The synthesised data are then analysed and transformed into different levels of recommendation according to the strength of evidence.

Part of the guideline will be presented and appropriate interpretation of the clinical evidence is emphasised (eg randomised controlled AED trials). The method and impact of guideline dissemination will also be discussed.

Ching-wan Lam

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There are various ways of diagnosing genetic diseases. We can diagnose genetic diseases based on clinical criteria, radiological features, biochemical changes, and DNA sequence changes. DNA-based diagnosis of genetic disease is the preferred method because the fundamental abnormalities in genetic diseases are DNA sequence changes. Approximately half of the disease-causing mutations, such as frameshift mutations, initiation codon mutations, splicing mutations, lariat branch point mutation, stop codon mutations, mutation at polyadenylation sites, cryptic splice site mutations, DNA rearrangement, DNA duplication, actually affect the DNA sequences rather than affecting the function, stability or cellular trafficking of the gene products—the proteins. Clinical or biochemical phenotypes of genetic diseases could be variable—lack of genotype-phenotype correlations. Some non-DNA diagnostic testing may require invasive procedures and the corresponding assays may only be available in few (research) laboratories in the world.

In the past decades, we have performed mutational analysis of a number of genes related to neurogenetic diseases, namely Parkinson's disease, primary torsion dystonia, dopa-responsive dystonia, Huntington's syndrome, Kennedy syndrome, MELAS, Leigh syndrome, hereditary spastic paraplegia, and porphyria. In all these studies, a direct mutation detection and identification was employed. A diagnostic method based on direct detection of genetic mutation is: (1) fundamental, definitive, objective, ultimate, and predictive; (2) 100% sensitive and specific in distinguishing heterozygotes from normal individuals; (3) 100% sensitive and specific in identification of presymptomatic family members; (4) crucial for reproductive and genetic counselling. If the disease-causing gene is known for a heritable disease, simply giving the chance 0.25 for recurrence of an autosomal recessive disease probably cannot satisfy our patients in the post-genomic era. For autosomal dominant disease, the chance of recurrence is 0.5, and is too high to be accepted by most parents or patients. For clinicians, DNA-based testing of genetic disease can prevent misdiagnosis and increasing our confidence in diagnosing the rare diseases.

## **Neurotoxicology**

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Some of the naturally occurring or synthetic chemical agents can affect the structure, function, development, and regenerative capacity of the central and peripheral nervous system. In adults, the central nervous system is protected by the blood-brain barrier. It effectively retards the transfer of charged and large-molecular-weight compounds from the circulation to nervous tissue. However, it does not provide protection against lipid-soluble agents or toxic agents that damage the blood-brain barrier. The targets of neurotoxins include the neuron (cell body), axon, myelinating cell and neurotransmitter system. Acute exposure to high doses or prolonged exposure to low concentrations of a neurotoxin can result in neuronopathy, axonopathy, myelinopathy and transmission toxicity. It is common practice to consider neurotoxic diseases in terms of the toxic agents (eg heavy metals, organophosphate insecticides) or their clinical presentations (eg encephalopathy, peripheral neuropathy). The clinical signs and symptoms of neurotoxin exposure may be expressed in the central, the peripheral and the autonomic nervous systems and in skeletal muscles. A careful history, detailed clinical examination, behavioural tests, biochemical tests, EEG, pathologies and epidemiological studies can be used to detect neurotoxicity. In Hong Kong, neurotoxins from marine dinoflagellates are important causes of seafood-poisoning syndromes such as ciguatera and paralytic shellfish poisoning. Both lead and methylmercury are neurotoxic, particularly to the developing brain. With respect to methylmercury, the primary source of exposure is fish consumption. It is important to remember the beneficial effects of fish consumption (in adults, children and pregnant women) and the provisional tolerable weekly intake to protect the developing foetus, the most sensitive subgroup of the population. Herbs such as the *Aconitum* species contain neurotoxins.

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Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurobehavioural childhood disorders. This disorder is characterised by pervasive inattentiveness, distractibility, impulsivity, and age-inappropriate hyperactivity that often results in substantial functional impairment. It affects 3 to 5% of all children.

The aetiology of ADHD remains unknown; however, the genetic cause is likely to play an important role. An analysis of 20 independent twin studies demonstrated 76% heritability of ADHD. Risk of having ADHD is also increased substantially if a first-degree relative is also diagnosed (including parents and siblings). At present, no genetic tests can be used to reliably predict the disorder. Brain imaging techniques, including PET, structural MRI, and fMRI, have rapidly advanced our understanding of the specific brain regions that include parts of the cerebellum and circuits that connect the frontal lobe and striatum, as involved in the pathophysiology of ADHD.

The American Academy of Child and Adolescent Psychiatry has published guidelines for the assessment and treatment of children and adolescents with ADHD. The recommendation provides information regarding clinical evaluation for ADHD, comorbid conditions associated with ADHD, research on the aetiology of the disorder, and psychopharmacologic and psychosocial interventions for ADHD. Stimulants are frequently the initial psychopharmacologic treatment. Each patient has a unique medication dose-response curve. Most patients will require increases in dosing as treatment continues. Close monitoring for treatment-emergent side-effects is important. The FDA has issued a black box warning concerning the use of stimulants to treat ADHD in patients with structural cardiac abnormalities, but for children and adolescents with no cardiac risks, stimulants are safe and effective.

With more and more studies confirming that ADHD persists from adolescence to adulthood, adult ADHD emerged as a unique malady in its own right. Despite this shift in attitude, a significant number of obstacles in the evaluation of the adult with ADHD remain.

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