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### 3rd Hong Kong Neurological Congress cum 26th Annual Scientific Meeting of The Hong Kong Neurological Society

Council of The Hong Kong Neurological Society	4
Organising Committee	4
List of Speakers	5
Scientific Programme	6

SESSION	ABSTRACT	PAGE
<b>FREE PAPER PRESENTATIONS</b>		
<b>Pilot Study for Subgroup Classification for Autism Spectrum Disorder Based on Dysmorphology and Physical Measurements in Chinese Paediatric and Adolescent Population</b> <i>Polly TY Wong, Virginia CN Wong</i>	FP 1	9
<b>Promotion of Physical Activity and Fitness in the Parki-Fit &amp; Walk Program Addressing the Non-motor Symptom 'Fatigue' for Idiopathic Parkinson's Disease</b> <i>CM Kwok, HT Lui, LF Hui, KY Wong</i>	FP 2	10
<b>Cryptococcal Meningitis</b> <i>Helen Yip, MC Kwan, WK Cheng, WY Lau, KF Ko</i>	FP 3	11
<b>A Young Lady with Artery of Percheron Infarction and Patent Foramen Ovale</b> <i>SH Li, TY Wai, MF Ip, KK Ma</i>	FP 4	12
<b>Clinical and Genetic Evaluation of 23 Children with Infantile-onset Epileptic Encephalopathy</b> <i>Alvin CC Ho, Anna KY Kwong, CW Fung, Virginia CN Wong</i>	FP 5	13

<b>DISSERTATION HIGHLIGHTS</b>		
<b>Morbidity and Mortality of Guillain-Barré Syndrome in Hong Kong</b> <i>Anna HY Wong</i>	DH 1	14
<b>Intracerebral Haemorrhage in Patients Warfarinised for Non-valvular Atrial Fibrillation (NVAf) and the Use of HAS-BLED Score in Addition to CHA2DS2-VASc Score to Refine the Decision on Anticoagulation for NVAf Patients</b> <i>MK Fong</i>	DH 2	14

SESSION	ABSTRACT	PAGE
<b>Study on the Safety and Efficacy of Dabigatran Etexilate (Pradaxa®) in Stroke Prevention on Hong Kong Chinese with Atrial Fibrillation as Compared with Warfarin: a Local Hospital Experience</b> <i>KK Ma</i>	<b>DH 3</b>	15
<b>Acute Ischaemic Stroke in Patients with Atrial Fibrillation and Their Use of Warfarin</b> <i>Eric YC Leung</i>	<b>DH 4</b>	16
<b>SYMPOSIUM ON STROKE</b>		
<b>Recent Advances in Stroke Imaging</b> <i>PW Cheng</i>	<b>S 1</b>	17
<b>Intracranial Stenting</b> <i>WM Lui</i>	<b>S 2</b>	18
<b>SYMPOSIUM ON EPILEPSY</b>		
<b>Clinical Use of Electroencephalography: Ten Years After the Millennium</b> <i>Ziyi Chen</i>	<b>S 3</b>	19
<b>The Mechanism of Neural Tube Defects Induced by Antiepileptic Drugs</b> <i>Liemin Zhou</i>	<b>S 4</b>	19
<b>Ketogenic Diet / Modified Atkin's Diet for Epilepsy</b> <i>Phyllis YP Yau, Eva LW Fung</i>	<b>S 5</b>	20
<b>SYMPOSIUM ON MOVEMENT DISORDERS AND NEURODEGENERATION</b>		
<b>Management of Gait Disorders in Parkinson's Disease: a Neurologist's Perspective</b> <i>Germaine HF Chan</i>	<b>S 6</b>	20
<b>Rehabilitation of Gait Disorders in Parkinson's Disease</b> <i>Margaret Mak</i>	<b>S 7</b>	21
<b>The Therapeutic Effect of Hepcidin in Parkinson's Disease Via Regulation of Brain Iron and <math>\alpha</math>-Synuclein Accumulation</b> <i>Ya Ke</i>	<b>S 8</b>	21
<b>Mechanism of Deep Brain Stimulation in Parkinsonism: Direct Involvement of the Primary Motor Cortex</b> <i>WH Yung</i>	<b>S 9</b>	22
<b>SYMPOSIUM ON DEMENTIA AND NEURODEGENERATION</b>		
<b>Spinocerebellar Ataxia in Chinese</b> <i>Anne YY Chan, Edwin HY Chan</i>	<b>S 10</b>	23
<b>Individualised Stem Cell Therapy</b> <i>Ken KL Yung</i>	<b>S 11</b>	24
<b>Identification and Characterisation of a Cognitive Enhancer from Traditional Chinese Medicine</b> <i>Fanny CF Ip, Nancy Y Ip</i>	<b>S 12</b>	24

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SESSION	ABSTRACT	PAGE
<b>LUNCH SYMPOSIUM</b>		
<b>Treatment of Refractory Multiple Sclerosis</b> <i>Finn Sellebjerg</i>	<b>S 13</b>	25
<b>SYMPOSIUM ON NEUROLOGIC INFECTION</b>		
<b>Intracranial Abscesses and Infections of Neurosurgical Shunts and Drains</b> <i>YW Fan</i>	<b>S 14</b>	25
<b>The 'Not So Common' Causes of Central Nervous System Infection in Hong Kong: Diagnoses You Cannot Afford to Miss</b> <i>Jasper FW Chan</i>	<b>S 15</b>	26
<b>SYMPOSIUM ON NEUROLOGY HIGHLIGHT</b>		
<b>Ten Minutes Vestibular Examinations but Persistent Rehabilitative Exercises</b> <i>Dennis KK Au</i>	<b>S 16</b>	26
<b>Neurostimulation in Primary Headache Disorders</b> <i>Raymond CK Chan</i>	<b>S 17</b>	27
<b>Late-onset Pompe Disease in the New Enzyme Replacement Therapy Era</b> <i>Bun Sheng</i>	<b>S 18</b>	27
<b>POSTERS</b>		
<b>Experience of Using Intravenous Thrombolysis in Elderly Patients with Major Acute Ischaemic Stroke in Kwong Wah Hospital</b> <i>Helen Yip, MC Kwan, WK Cheng, WY Lau, KF Ko, TY Chan, ML Lai</i>	<b>P 1</b>	28
<b>Griffiths Mental Developmental Scales Validation for Chinese Children</b> <i>Winnie WY Tso, LI Ao, M Li, X Zhang, FY Jiao, X Xu, KX Du, XL Xia, Denise Challis, Virginia CN Wong</i>	<b>P 2</b>	28
<b>The Prognosis of Acute Symptomatic Seizures after Ischaemic Stroke</b> <i>T Leung, H Leung, Y Soo, C Leung, V Mok, KS Wong</i>	<b>P 3</b>	29
<b>INDEX</b>		30

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## List of Speakers

Name	Affiliation
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# SCIENTIFIC PROGRAMME

VENUE: LECTURE HALL, 7/F, BLOCK H, PRINCESS MARGARET HOSPITAL, HONG KONG SAR

2 NOVEMBER 2013, SATURDAY

08:30 – 09:00	Registration	Lobby <b>POSTER PRESENTATION</b>
09:00 – 10:15	<b>FREE PAPER PRESENTATION</b> <i>Chairpersons: Wing-keung Cheng, Winnie Wing-yin Wong</i>	
10:15 – 10:45	Coffee Break / Poster Viewing	
10:45 – 12:15	<b>DISSERTATION HIGHLIGHTS</b> <i>Chairpersons: Wing-keung Cheng, Winnie Wing-yin Wong</i>	
12:15 – 13:00	Lunch	
13:00 – 13:15	<b>OPENING CEREMONY</b> Guest of Honour: <i>The Hon Dr Wing-man Ko, BBS, JP, Secretary of Food and Health</i>	
13:15 – 14:45	<b>SYMPOSIUM ON STROKE</b> <i>Chairpersons: Chen-ya Huang, Chun-ming Cheung</i> <b>Recent Advances in Stroke Imaging</b> <i>PW Cheng</i> <b>External counterpulsation</b> <i>Thomas WH Leung</i> <b>Intracranial Stenting</b> <i>WM Lui</i>	
14:45 – 15:05	Coffee Break	
15:05 – 16:35	<b>SYMPOSIUM ON EPILEPSY</b> <i>Chairpersons: Jason Ka-yeung Fong, Eric Lok-yiu Chan</i> <b>Clinical Use of Electroencephalography: Ten Years After the Millennium</b> <i>Ziyi Chen</i> <b>The Mechanism of Neural Tube Defects Induced by Antiepileptic Drugs</b> <i>Liemin Zhou</i> <b>Ketogenic Diet / Modified Atkin's Diet for Epilepsy</b> <i>Phyllis YP Yau, Eva LW Fung</i>	
18:00	Faculty Dinner (by invitation only)	

### 3 NOVEMBER 2013, SUNDAY

<b>08:30 – 09:00</b>	Registration	Lobby <b>POSTER PRESENTATION</b>
<b>09:00 – 10:30</b>	<b>SYMPOSIUM ON MOVEMENT DISORDERS AND NEURODEGENERATION</b> <i>Chairpersons: Mandy Au-yeung, Kin-lun Tsang</i> <b>Management of Gait Disorders in Parkinson's Disease: a Neurologist's Perspective</b> <i>Germaine HF Chan</i> <b>Rehabilitation of Gait Disorders in Parkinson's Disease</b> <i>Margaret Mak</i> <b>The Therapeutic Effect of Hepcidin in Parkinson's Disease Via Regulation of Brain Iron and <math>\alpha</math>-Synuclein Accumulation</b> <i>Ya Ke</i> <b>Mechanism of Deep Brain Stimulation in Parkinsonism: Direct Involvement of the Primary Motor Cortex</b> <i>WH Yung</i>	
<b>10:30 – 10:50</b>	Coffee Break	
<b>10:50 – 12:20</b>	<b>SYMPOSIUM ON DEMENTIA AND NEURODEGENERATION</b> <i>Chairpersons: Vincent CT Mok, Ken KL Yung</i> <b>Spinocerebellar Ataxia in Chinese</b> <i>Anne YY Chan, Edwin HY Chan</i> <b>Individualised Stem Cell Therapy</b> <i>Ken KL Yung</i> <b>Identification and Characterisation of a Cognitive Enhancer from Traditional Chinese Medicine</b> <i>Fanny CF Ip, Nancy Y Ip</i>	

(Cont'd on p.8)



12:20 – 12:50	Lunch	Lobby <b>POSTER PRESENTATION</b>
12:50 – 13:40	<b>LUNCH SYMPOSIUM</b> <i>Chairperson: Kwok-kwong Lau</i> <b>Treatment of Refractory Multiple Sclerosis</b> <i>Finn Sellebjerg</i> <b>Case Sharing</b> <i>Alexander YL Lau</i>	
13:40 – 15:10	<b>SYMPOSIUM ON NEUROLOGIC INFECTION</b> <i>Chairpersons: Richard Kay, Alan CT Tse</i> <b>Neurological Vignette of HIV-infected Patients</b> <i>Patrick CK Li</i> <b>Intracranial Abscesses and Infections of Neurosurgical Shunts and Drains</b> <i>YW Fan</i> <b>The 'Not So Common' Causes of Central Nervous System Infection in Hong Kong: Diagnoses You Cannot Afford to Miss</b> <i>Jasper FW Chan</i>	
15:10 – 15:25	Coffee Break	
15:25 – 16:55	<b>SYMPOSIUM ON NEUROLOGY HIGHLIGHT</b> <i>Chairpersons: Shi-hon Ng, Bun Sheng</i> <b>Ten Minutes Vestibular Examinations but Persistent Rehabilitative Exercises</b> <i>Dennis KK Au</i> <b>Neurostimulation in Primary Headache Disorders</b> <i>Raymond CK Chan</i> <b>Late-onset Pompe Disease in the New Enzyme Replacement Therapy Era</b> <i>Bun Sheng</i>	
16:55 – 17:05	Closing Remarks & Award Presentation	

## Pilot Study for Subgroup Classification for Autism Spectrum Disorder Based on Dysmorphology and Physical Measurements in Chinese Paediatric and Adolescent Population

Polly TY Wong, Virginia CN Wong

Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong SAR

**Background:** Autism spectrum disorder (ASD) is defined as a range of complex neurodevelopmental disorder affecting individuals along a continuum of severity in communication, social interaction and behaviour. The impact of ASD significantly varies among individuals, and the cause of ASD can originate broadly between genetic and environmental factors. Previous ASD researches indicate that early identification combined with a targeted treatment plan involving multidisciplinary therapies and behavioural interventions can bring about substantial improvement to the development of autistic patients. Currently there is no cure for ASD, and the clinical variability and uncertainty of the disorder still remains. Hence, the search to unravel heterogeneity within ASD by subgroup classification may provide clinicians with a better understanding of ASD and allow for a more definitive course of action.

**Methods:** In this study, a norm of physical measurements including height, weight, head circumference, ear length, outer and inner canthus, interpupillary distance, philtrum, hand and foot length were collected from 658 normal Chinese children aged 1 to 7 years. The norm collected was compared against 80 Chinese ASD children aged 1 to 12 years. We attempted to find subgroups within ASD subjects based on identifying physical abnormalities; individuals were classified as (non)dysmorphic with the Autism Dysmorphology Measure (ADM) Scoring Algorithm from physical examinations.

**Results:** Our results showed that there was a significant difference ( $P < 0.05$ ) between age-matched normal controls and ASD group in measurements for head circumference, outer and inner canthus, philtrum length, right and left foot length. Within the 80 ASD patients, 39 were defined as dysmorphic ( $P = 0.00$ ).

**Conclusion:** This study attempted to identify subgroups within ASD patients based on physical measurements and dysmorphology examinations. The information from this study seeks to benefit ASD community by identifying the possible subtypes of ASD in Chinese preschool population, and to seek for a more definitive diagnosis, referral, and treatment plan.

## Promotion of Physical Activity and Fitness in the Parki-Fit & Walk Program Addressing the Non-motor Symptom 'Fatigue' for Idiopathic Parkinson's Disease

FP 2

CM Kwok<sup>1</sup>, HT Lui<sup>2</sup>, LF Hui<sup>2</sup>, KY Wong<sup>1</sup>

<sup>1</sup> Physiotherapy Department, Integrated Rehabilitation Services, Tseung Kwan O Hospital, Hong Kong SAR

<sup>2</sup> Division of Neurology, Department of Medicine, Tseung Kwan O Hospital, Hong Kong SAR

**Introduction:** Idiopathic Parkinson's disease (iPD) is often complicated with various motor and non-motor symptoms, which has great impact in daily functions, fitness, and quality of life (QoL) wellbeing. Fatigue is one of the common irritating non-motor symptoms. It often appears as an obstacle to daily physical exercise adherence. However, limited clinical research addressed its impacts during the process of rehabilitation.

**Objectives:** (1) To evaluate the impact of non-motor symptom, fatigue, on health fitness, QoL and amount of physical activity after participating the Parki-Fit & Walk Program; and (2) to determine the predicting factors contributing to the change of endurance capacity through physical exercise in daily living.

**Methods:** After iPD patients received pharmacological control from Neurology Clinic and Integrated PD Service, indicated patients will be recruited in the Parki-fit & Walk Program for 6 months. It was designed for multifaceted behavioural change with various strategies to achieve better QoL and health fitness, via promoting active lifestyle towards moderate physical activity level. The amount of physical activity was measured by a standardised 7-day recall questionnaire (Physical Activity Recall Questionnaire [PARQ]). Details of program workflow include 20 iPD patients in the 'fatigue' group (FG) and 26 in the 'non-fatigue' group (NFG). They were identified by employing the 9-item Fatigue Severity Scale (FSS), which reflected physical and mental fatigue. The individual score of the mean of the numerical responses was calculated; a cut-off of 4 was used to select fatigued from non-fatigued.

**Results:** The NFG increased by 70% and the FG increased by 49.6% in total energy expenditure of moderate physical activities ( $P=0.001$ ; repeated measured ANOVA) after intervention. They all achieved the recommended moderate physical exercise level. Both groups obtained obvious health fitness gain. Motor control (UPDRS motor score) improved by 33% in NFG and 6.4% in FG; walking endurance (6-minute walk distance) improved by 32.5% in NFG and 0.6% in FG; comfort gait speed improved by 33.8% in NFG and 4.3% in FG; QoL wellbeing (Motor score in Parkinson's disease 39 Questionnaire) improved by 67.4% in NFG and 6.4% in FG ( $P=0.001$ ; repeated measured ANOVA). The linear stepwise multivariate regression analysis showed the change of walking endurance was associated with change of gait speed and change of moderate level physical exercises ( $P=0.000$ ). This model predicted 61% correctly ( $R^2=0.61$ ). The change of endurance capacity can be predicted by the following equation:  $15.24 + 161.168 \times \text{change of gait speed} + 0.05 \times \text{change of moderate level physical exercises energy expenditure}$  ( $n=46$ ,  $R^2=0.61$ ,  $P=0.000$ ).

**Conclusion:** The study suggested that early multidisciplinary team approach included comprehensive evaluation, customised disease management and training program like the Parki-fit & Walk Program will facilitate holistic care in iPD. Determining the fatigue level may facilitate specialised education, exercise dosage prescription, and program adherence. Further researches are recommended to study its long-term effect on health care outcomes.

Helen Yip, MC Kwan, WK Cheng, WY Lau, KF Ko  
Department of Medicine and Geriatrics, Kwong Wah Hospital, Hong Kong SAR

We report a case of cryptococcal meningitis in an immunocompetent male presented with fever for 4 months despite extensive work-up.

A 63-year-old man Hong Kong resident who is a retired shopkeeper with a medical history of hypertension and lumbar spondylosis. He presented to our Medical Unit for mental dullness with decreased short-term memory. Before current admission, the patient was admitted to Our Lady of Maryknoll Hospital for 4-month history of pyrexia and recently diagnosed pulmonary cryptococcal infection confirmed with lung biopsy being put on 4 days of fluconazole therapy prior to current admission.

On examination, the patient was afebrile with a Glasgow Coma Scale score of E4M6V4. Neck rigidity was negative. Limb muscle power was equal and symmetrical. Plantars were bilaterally flexor. Laboratory investigations revealed raised total leukocyte count (white cell count [WCC],  $15 \times 10^9/L$ ). Blood for renal function tests and liver function tests were normal. Cerebrospinal fluid (CSF) examination revealed WBC  $168/cm^3$  with predominantly lymphocytes 67%, with protein of 7.03 g/L and glucose of 0.9 mmol/L (corresponding blood glucose was 6.0 mmol/L).

There were no microorganisms on Gram and Ziehl-Neelsen (Z-N) stains. India ink examination was negative with a negative growth on bacterial culture. The CSF and serum cryptococcal antigen were positive, with a titre of 1:256 with culture yield *Cryptococcus neoformans*.

A computed tomography (CT) scan of the brain showed hypodensity over right caudate nucleus and Lt pontine area. Mini-Mental State Examination (MMSE) was 19 out of 30 on admission. His complement and immunoglobulin levels were within normal limits. Anti-HIV antibody was negative in two blood samples 3 months apart.

He was started on antifungal pharmacotherapy with amphotericin B with addition of flucytosine (5FC) as induction therapy. Subsequent MMSE was 26 out of 30 after 3 weeks of antifungal treatment. Fluconazole was followed as consolidation and maintenance therapy.

Most cases of cryptococcal meningitis occur in immunocompromised patients but it has been reported in HIV-negative patients caused by chemotherapy-related immunosuppression, history of organ transplantation, haematological malignancies, concurrent use of corticosteroid therapy, and sarcoidosis. Occasionally, no obvious underlying cause can be detected.

Cryptococcal meningitis remains a devastating disease with a high mortality. An important predictor of early mortality is an abnormal mental status at presentation and mortality can be up to 25%. Other prognostic factors include baseline high-opening pressure, poor WCC response in CSF, high CSF titres of cryptococcal antigen  $>1024$ , positive blood culture and CSF India ink/Gram stain positivity.

Our patient had a gradual improvement in cognition and mobility after prompt treatment. Early diagnosis and management is essential to hasten recovery in cryptococcal meningitis.

SH Li, TY Wai, MF Ip, KK Ma

Department of Medicine, North District Hospital, Hong Kong SAR

A 30-year-old woman attended Neurology Clinic at North District Hospital in March 2010 for investigation of diplopia. She complained of a period of impaired consciousness followed by diplopia in 2003 when she was in Mainland China. She reported gradual recovery afterwards though residual diplopia remained. She had no head or neck injury. She enjoyed good past health.

Neurological examination showed impaired downward gaze (pursuit and saccade). Other parts of examination were unremarkable. She did not have any limb weakness or ataxia. Her cognitive was unremarkable. Computed tomographic non-contrast brain revealed bilateral thalamic and anterior midbrain old infarcts (Fig 1). Electrocardiogram and chest X-ray were normal. Blood tests for fasting glucose, lipid, renal and liver function test, complete blood picture, clotting, erythrocyte sedimentation rate were normal. Immune markers (ANA, DNA, ENA, and ANCA) were negative. Anti-cardiolipin antibody, protein C and S, and anti-thrombin III were also normal. Magnetic resonance imaging of the brain showed old infarcts at bilateral paramedian thalami and left rostral midbrain (Figs 2 and 3) suggesting old infarction from occlusion of artery of Percheron. Moreover, multiple lacunar infarcts were noted in bilateral corona radiata, frontal and parietal white matter, left temporal lobe and left centrum semiovale. Magnetic resonance angiography of the cerebral, carotid and vertebral arteries were unremarkable (Fig 4). Thorough investigations for her young stroke including carotid duplex ultrasound and transcranial Doppler (TCD) ultrasound, transthoracic echocardiogram as well as Holter test were all unremarkable. Bubble TCD was then performed that revealed one microembolic signal after Valsalva manoeuvre suggestive of low-grade right-to-left shunt. Transesophageal echocardiogram was finally performed which confirmed the presence of patent foramen ovale that can account for her prior stroke.

She has been given clopidogrel 75 mg daily orally since 2010 as she has aspirin allergy. She delivered a normal baby uneventfully in June 2011. She has not had stroke recurrence.

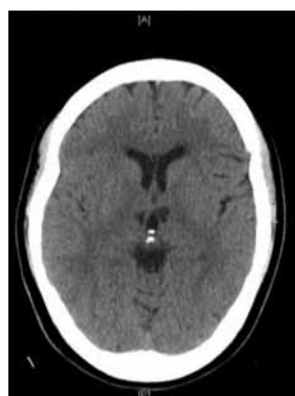


Fig 1

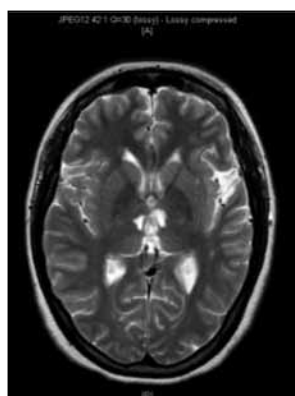


Fig 2

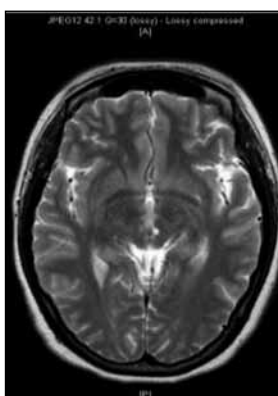


Fig 3



Fig 4

Alvin CC Ho, Anna KY Kwong, CW Fung, Virginia CN Wong

Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Queen Mary Hospital / Duchess of Kent Children's Hospital, Hong Kong SAR

**Background:** Infantile epileptic encephalopathies (IEE) are a group of conditions in which cognitive, sensory, and/or motor functions deteriorate as a consequence of epileptic activities, which consist of frequent seizures and/or major interictal paroxysmal activity. There are various causes of IEE and they may occur at any age.

**Methods:** We reviewed patients in the Department of Paediatrics and Adolescent Medicine of the University of Hong Kong, Queen Mary Hospital and Duchess of Kent Children's Hospital with the clinical diagnosis of IEE of unknown aetiology over a 10-year period (2003-2012). Five genes (*ARX*, *CDKL5*, *KCNQ2*, *SCN1A*, and *STXBP1*) were screened using sequencing.

**Results:** A total of 23 patients were identified and their electroclinical features were studied. Of the 23 patients, 10 (43.5%) had epileptic spasm as the presenting seizure type. Throughout the clinical course, patients were characterised by frequent seizures that were multifocal and pharmaco-resistant. The commonest subsequent seizure type was generalised tonic/clonic/tonic-clonic seizure (17 out of 23, 73.9%). All of the patients had developmental delay of various degrees. Movement disorder in terms of dystonia was the most common associated clinical feature (10 out of 23, 43.5%). Five genes (*ARX*, *CDKL5*, *KCNQ2*, *SCN1A*, and *STXBP1*) were screened in 20 of our patients. We identified three patients with *STXBP1* mutations, two patients with *SCN1A* mutations, and one patient with *KCNQ2* mutation. The overall detection rate was 30% (6/20). Two out of three patients with Dravet phenotype were screened positive for *SCN1A* mutation. The only patient with typical Ohtahara phenotype was screened positive for *STXBP1* mutation.

**Conclusion:** This study highlighted the clinical characteristics of IEE and studied the yield of mutational screening of five selected genes in this group of patients. Dravet syndrome and Ohtahara syndrome have characteristic phenotypes. *SCN1A* and *STXBP1* mutational analysis should be performed in children with classic presentations of the above-named conditions respectively.

Anna HY Wong

Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

**Objectives:** To review the clinical profile and outcome of patients with Guillain-Barré syndrome (GBS) managed in hospitals in Hong Kong and to look for any predictors for mechanical ventilation, poor disability outcome, and mortality.

**Methods:** Subjects suffering from GBS admitted to Queen Elizabeth Hospital, Princess Margaret Hospital, and Caritas Medical Centre from January 2001 to December 2010 were included. Patients younger than 18 years old or suffering from neuropathy other than GBS or incomplete medical record available for review were excluded. A multivariate analysis was used for analysis of predictors of outcome.

**Results:** A total of 104 patients were included. When comparing between cohorts of three hospitals, they showed similar baseline characteristics and outcome. Higher Erasmus GBS outcome score and Erasmus GBS respiratory insufficiency score were associated with poorer outcome, though the association was not always statistically significant among three cohorts. GBS disability score on admission and age were significant predictors of mechanical ventilation (odds ratio=3.0; 95% confidence interval, 1.64-5.52;  $P<0.0001$ ) and mortality (odds ratio=1.1; confidence interval, 1.03-1.17;  $P=0.007$ ), respectively. No significant predictor could be identified for independency of daily living at 6 months.

**Conclusion:** The median age and mortality rate of GBS in Hong Kong was higher when compared to those of previous studies. Among the three local hospitals studied, baseline characteristics and outcome were similar. Age and GBS disability score on admission were significantly related to mortality and risk of mechanical ventilation respectively while Erasmus GBS outcome score and Erasmus GBS respiratory insufficiency score on admission can serve as a reference in predicting outcome of patients with GBS.

## Intracerebral Haemorrhage in Patients Warfarinised for Non-valvular Atrial Fibrillation (NVAF) and the Use of HAS-BLED Score in Addition to CHA2DS2-VASc Score to Refine the Decision on Anticoagulation for NVAF Patients

MK Fong

Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong SAR

**Background:** Atrial fibrillation (AF) can result in catastrophic thromboembolic complications. Warfarin reduces thromboembolic risk but is underutilised for the fear of major bleeding. CHA2DS2-VASc and HAS-BLED scores are helpful for risk stratification.

**Objectives:** Part I—To compare the CHA2DS2-VASc and HAS-BLED scores among warfarinised non-valvular AF (NVAF) patients with and without intracerebral haemorrhage (ICH). Part II—To study the clinical course and outcome of warfarin-related ICH.

**Methods:** Three patient groups in Princess Margaret Hospital (PMH), Queen Elizabeth Hospital (QEH), and Caritas Medical Centre (CMC) were retrospectively studied: Case—warfarinised NVAF patients with ICH (PMH/QEH/CMC) during 1 January 2006 to 31 December 2011; Part I reference—warfarinised NVAF patients (PMH) without ICH during 1 July 2011 to 31 October 2011; Part II control—non-warfarin ICH patients (PMH) matched with the case group for gender, age ( $\pm 1$  year), and admission year, in one-to-one ratio.

**Results:** In Part I, 114 cases and 661 references were recruited. The case group had a higher median CHA2DS2-VASc score (5 vs 4;  $P=0.011$ ) and more patients in high-bleeding risk category than reference group (46.5% vs 36.6%;  $P=0.033$ ). Most anticoagulated patients (99.1%) had appropriate benefit-risk balance. In Part II, the mean admission international normalised ratio (INR) was 2.8. Eighty-two (73.2%) patients had ICH despite admission INR did not exceed therapeutic range ( $\text{INR} \leq 3.0$ ). Initial ICH volumes were comparable among case and control groups. A majority of patients in both groups had poor functional outcome at 6 months. Warfarin-related ICH had a higher in-patient mortality (51.8% vs 36.0%;  $P=0.02$ ) and 6-month mortality (60.5% vs 43%;  $P=0.01$ ) than non-warfarin ICH. Lower admission Glasgow Coma Scale score ( $P=0.001$ ), higher initial ICH volume ( $P=0.003$ ), and higher ICH score ( $P<0.001$ ) were predictors of poor outcome.

**Conclusion:** Warfarin-related ICH in NVAF patients had significant morbidity and mortality. CHA2DS2-VASc score and HAS-BLED score are useful risk stratification tools to guide treatment in NVAF patients.

## Study on the Safety and Efficacy of Dabigatran Etexilate (Pradaxa®) in Stroke Prevention on Hong Kong Chinese with Atrial Fibrillation as Compared with Warfarin: a Local Hospital Experience

KK Ma

Department of Medicine, North District Hospital, Hong Kong SAR

**Background:** The use of anticoagulant for stroke prevention in atrial fibrillation is raising concern in Hong Kong. Warfarin was the only oral anticoagulant available in the market before the launch of dabigatran etexilate. The benefit of new anticoagulant is reported as non-inferior to warfarin on stroke prevention. Besides, patients would benefit from less food-and-drug restriction in view of relative less interaction. Thus, it can provide a relative stable anticoagulation effects compared with warfarin. However, there are no local data on the efficacy and safety on the use of dabigatran etexilate in Hong Kong.

**Objective:** To study the safety and efficacy of dabigatran etexilate in stroke prevention on Hong Kong Chinese with atrial fibrillation.

**Methods:** This was a retrospective phase IV postmarket study. Patients on dabigatran etexilate from medical specialist out-patient clinic in North District Hospital between January 2009 and August 2012 were recruited in the study. The safety issue of the dabigatran etexilate was defined as the incidence of major bleeding including intracranial haemorrhage, and minor bleeding, gastro-intestinal complications and hypersensitivity reaction. The efficacy of the dabigatran etexilate was investigated by patient outcomes. The primary outcome was recurrent ischaemic stroke or transient ischaemic attack. The secondary outcome was the mortality incidence. The overall data were compared with Asian and non-Asian data from RELY study upon the dabigatran treatment arms and warfarin arm. The data were reviewed by February 2013.

**Results:** A total of 96 patients were enrolled in the study. The mean follow-up period was 16 months. Our patients were more advance in age and multiple co-morbidities with higher CHADS2 scores. The stroke rate was 3.37% per year which was higher when compared with the dabigatran treatment and warfarin arm in RELY study as 1.39% and 2.50% per year, respectively. Four patients got interrupted dabigatran use before the stroke events. The mortality rate was 3.37% per year as compared with dabigatran treatment and warfarin arm in RELY study as 4.01% and 5.01% per year, respectively. The major and minor bleeding risks were 4.69% and 1.56%, respectively, which were lower when compared with the dabigatran treatment arm and warfarin arm in RELY study.

**Conclusions:** The mortality and major adverse event rates were comparable between our study data and the RELY study in the Asian group and non-Asian group. The higher stroke rate in our study may be related to the interrupted dabigatran use such as prolonged drug withdrawal before procedure, after minor bleeding or inappropriate dosage. Further study with larger sample size, longer study period, and comparable control arm are recommended.



Eric YC Leung

Department of Medicine, Ruttonjee Hospital, Hong Kong SAR

**Objectives:** Atrial fibrillation (AF) is a strong independent risk factor for ischaemic stroke (IS). Current guidelines suggest anticoagulation as a class 1A recommendation for patients with IS and AF (IS/AF). We investigated any difference between IS patients with and without AF, and factors associated with their initiation and continuation of warfarin.

**Methods:** A cross-sectional retrospective study utilising the stroke registry of Pamela Youde Nethersole Eastern Hospital from 2009 to 2010 was conducted. A total of 824 IS patients with AF (n=216) and without AF (n=608) were examined for difference in demographics, stroke subtypes, stroke severity, treatments, and outcomes. Univariate analysis was used to determine any association(s) with increased likelihood of 1-year re-stroke or death. Warfarin prescription, its use against the CHADS2 scores, reason(s) for not prescribing warfarin, warfarin initiation and termination in the year post-discharge were examined in IS/AF patients.

**Results:** Our IS/AF patients were older, more likely to be female, to have ischaemic heart disease and more severe stroke, to receive acute thrombolysis, and were more disabled by their stroke. A NIHSS score of  $\geq 5$  on discharge, age  $\geq 80$  years, Glasgow Coma Scale score (GCS)  $\leq 12$ , and mRS  $\geq 4$  were associated with increased likelihood of 1-year mortality. Only 61 (32.1%) of the IS/AF patients were prescribed warfarin on discharge; warfarin prescription was highest in patients with CHADS2 score of 2. Nine (8.0%) of IS/AF patients not given warfarin on discharge (n=112) initiated warfarin and seven (11.5%) of the warfarinised patients (n=61) stopped warfarin, in the year following discharge. At 12 months, 58 (42.0%) patients were still using warfarin. The three most frequently documented reasons for not prescribing warfarin were poor functional status, no reason given, and bleeding risk. 60% of our warfarinised patients spent 100% time within international normalised ratio (INR) range of 1.5-3.0, but only 12% if the target INR range was 2.0-3.0.

**Conclusions:** The overall use of warfarin in our IS/AF patients remained low. Possible explanations include clinicians and patient perceptions of high complication(s) risk with warfarin and the underestimation of stroke risk from AF. Clinicians are encouraged to use the HAS-BLED score with the CHADS2 or CHA2DS2-VASc scores when considering patients for anticoagulation.

PW Cheng

Scanning Department, St Teresa's Hospital, Hong Kong SAR

With the advent of magnetic resonance (MR) and computed tomography (CT) imaging techniques, imaging has become an indispensable tool to the diagnosis and management of stroke patients. Advanced stroke imaging also plays a pivotal role in selection and monitoring of patients being treated by endovascular or intravenous intra-arterial recanalisation therapy.

Conventional MR imaging, especially the diffusion-weighted sequence, has vastly improved the sensitivity and specificity for detection of acute stroke as compared with CT scan in the early days. The first part of this talk will focus on the essential pearls and pitfalls in contemporary acute stroke imaging so as to improve diagnostic accuracy in our daily clinical practice by recognising common critical artefacts. Neuroimaging scores for acute stroke and intra-cerebral haemorrhage will also be briefly reviewed.

Secondly, the continually evolving multi-modality and multi-parametric stroke imaging approach will be elaborated. Advanced imaging techniques such as CT angiography, CT perfusion, dynamic susceptibility perfusion-weighted MR imaging, arterial spin-labelling perfusion-weighted MR imaging are increasingly employed for triage of patients for tailored acute stroke therapy as well as evaluation of chronic ischaemic stroke.

Emerging novel stroke imaging techniques such as diffusion tensor and permeability imaging will also be addressed in the context of their potential clinical application. The various directions for future stroke imaging research will be highlighted, including non-invasive vulnerable plaque imaging, recanalisation strategies over extended time window etc.

WM Lui

Department of Neurosurgery, Queen Mary Hospital, Hong Kong SAR

### ***Intracranial stent as an adjunct to endovascular embolisation/coiling***

Recent technological advances have led to the development of adjunctive devices and techniques to improve the results with endovascular embolisation/coiling. These are devices that help coils stay inside the aneurysm sac which can be particularly helpful for aneurysms with wide necks or large aneurysms that were difficult to treat with embolisation/coiling in the past.

One such adjunctive device is an intracranial stent. A stent is a metal mesh device in the shape of a pipe or tube which is placed inside the parent artery at the site of the aneurysm to cover the neck of the aneurysm. This helps to keep coils placed in the aneurysm sac to stay inside the sac.

The stents are usually made of nitinol, a high-grade metal alloy of nickel and titanium. One or more antiplatelet medicines such as aspirin, clopidogrel, ticlopidine, or others are required to prevent thromboembolism after stent placement. Therefore, the use of stent in emergency situation with prior antiplatelet coverage carries certain risk.

At the time of the embolisation/coiling procedure, or sometimes as a separate treatment, a microcatheter and wire are navigated from the access site (usually the femoral artery in the groin) using X-ray visualisation up to the site of the aneurysm in the brain. The stent can be pushed through the microcatheter and deployed at the intended target to cover the aneurysmal neck. Then another microcatheter is navigated through the stent strut and placed inside the aneurysm sac. Then coils are placed in the aneurysm sac as would be performed as described in the coiling description. The stent will prevent the coils from entering the parent artery and in so doing, a complete occlusion of the aneurysm sac is made possible.

### ***Flow diverters—pipeline embolisation device***

Approved by the Food and Drug Administration in April 2011, the pipeline embolisation device (PED) is a flexible mesh tube made of platinum and nickel-cobalt chromium alloy that can be used to block off large, giant, or wide-necked aneurysms in the intracranial arteries. The device can also reduce the likelihood that an aneurysm will rupture.

To implant the device, the pipeline is attached to the end of a catheter. The catheter is threaded into the carotid artery and into position at the aneurysm where the pipeline is expanded against the walls of the artery and across the neck of the aneurysm, cutting off blood flow to the aneurysm. The blood remaining in the blocked-off aneurysm forms a clot which reduces the likelihood the aneurysm will grow bigger or rupture. Aneurysms successfully treated with the pipeline will often shrink over time.

Ziyi Chen

Department of Neurology, The First Affiliated Hospital, Zhongshan (Sun Yat Sen) University, PR China

The electroencephalography (EEG), which is entirely harmless and relatively inexpensive, is the most important investigation in the diagnosis of epilepsies. In 2001, ILAE Task Force established a new diagnostic scheme for people with epileptic seizures and with epilepsy: ictal phenomenology, seizure type, syndrome, aetiology, and impairment. I am going to show some examples of clinical use of EEG in the new diagnostic scheme. First, the paroxysmal event should be differentiated between epileptic seizure and non-epileptic attack. Since the epileptic seizure has been defined as a transient occurrence of sign and/or symptoms due to abnormal excessive neuronal activity in the brain, synchronous EEG may be the key method for differentiation. We should pay attention to those patients with real epileptic seizure and pseudoseizures. Second, the type of epileptic seizures should be confirmed. Video-EEG is particularly important in the identification and categorisation of epileptic seizures. Here I am going to share both some typical cases of classic epileptic seizure types (such as generalised tonic-clonic seizure, absence seizure, atonic seizure), and some new types (such as eyelid myoclonia). Third, the epileptic syndrome or epileptic disease should be clearly diagnosed. The epileptic syndrome is defined as an epileptic disorder characterised by a cluster of signs and symptoms customarily occurring together. There are different characteristics in different epileptic syndrome. For example, electrical status epilepticus in sleep (ESES) is related to Landau-Kleffner syndrome (acquired epileptic aphasia) and epilepsy with continuous spike-and-waves during slow-wave sleep (ECSWS). In summary, EEG recording is of great diagnostic significance in clinical practices because it is associated with clinical manifestations.

## The Mechanism of Neural Tube Defects Induced by Antiepileptic Drugs

Liemin Zhou

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Neural tube defects (NTDs) are among the most prevalent and most severe congenital malformations worldwide. Polymorphisms in key genes involving the folate pathway have been reported to be associated with the risk of NTDs. Valproic acid (VPA) is one of the firstline antiepileptic drugs (AEDs) and widely used to control most subtypes of seizures. Some women with epilepsy during pregnancy need to be treated by VPA, which however will increase the risk of NTDs from the data of EURAP and the North American AED Pregnancy Registry. At present, the teratogenic mechanism induced by VPA is still unclear. Both the genetic polymorphism of folate metabolic enzymes and valproic acid therapy can affect gene transcription through histone hyperacetylation, DNA hypomethylation and the modulation of several transcription factors, which may play an important role in neural tube closure in sensitive patients via mediating the gene expression. In this lecture, we will analyse the role of genetic polymorphisms of folate metabolic enzymes, and DNA methylation and inhibition of histone deacetylases (HDACs) in NTDs induced by VPA, and explore the mechanism of NTDs caused by VPA.

Phyllis YP Yau<sup>1</sup>, Eva LW Fung<sup>2</sup>

<sup>1</sup>Dietetics Department and <sup>2</sup>Department of Paediatrics, Prince of Wales Hospital, Hong Kong SAR

Ketogenic diet has been used for treating epilepsy for almost 100 years. The utilisation and interests in the diet and its modification/variation are increasing in the past decade. With more clinical experience and scientific documentation of its efficacy, its uses have also been included in latest NICE guidelines. There are also reports of implementing the diet in the acute setting, especially in cases with super-refractory status epilepticus. Some of the greatest hurdles in implementing the ketogenic diet are the restriction in food intake, labour-intensive implementation, and maintenance of the diet and concerns on theoretical health risks associated with the diet. The development of less 'stringent' alternatives, like modified Atkins diet and low glycaemic index diet, have become much more attractive, especially for adults. They are much easier to implement and maintain, both for the patients and clinicians/dietitians. There is no restriction in mealtimes, calories, and liquid, etc. Studies have also demonstrated the efficacy in both children and adults. Besides uses in epilepsies, new applications of ketogenic diet therapies for other medical conditions have also been explored, including amyotrophic lateral sclerosis, diabetic neuropathy, and malignant brain tumours, etc.

## **Management of Gait Disorders in Parkinson's Disease: a Neurologist's Perspective**

Germaine HF Chan

Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

Gait and balance disorder is a common, yet debilitating problem in Parkinson's disease (PD) patients. The Sydney multicentre study showed a high fall risk of 87% in advanced PD patients, resulting in fractures and immobilisation. A recently published Chinese study also reproduced similar results. Therefore, it is important to understand the pathophysiological mechanism, detect the risk factors, and provide appropriate treatment.

### ***Pathophysiological mechanism of gait and balance disorders in Parkinson's disease***

Gait and balance dysfunction can occur in any stages of PD, even though it is more common in advanced PD patients. In early PD, dopamine deficiency accounts for these axial symptoms. Nonetheless, in advanced PD, gait disorder is more complex and is likely to involve both the dopaminergic and non-dopaminergic pathways. Besides, difficulty in multi-tasking, impaired sensorimotor integration, as well as a lack of compensatory stepping, may contribute to a higher incidence of falls in PD patients.

### ***Risk factors of falls in Parkinson's disease***

A history of two or more falls in the previous year is found to be the best predictive factor of falls in PD patients. Impaired ambulation, poor lower limb motor planning, and orthostasis also predict gait and balance problems.

### ***Management of gait and balance disorders in Parkinson's disease***

Axial symptoms in parkinsonism can be divided into two groups: dopamine responsive and dopamine resistant. In early PD patients, when dopamine deficiency is responsible for these symptoms, stepping up dopaminergic medications is the solution. In advanced PD patients, the gait disorders are more complicated and are often refractory to dopaminergic treatment. In this case, drugs targeting on the non-dopaminergic system, such as methylphenidate and amantadine, may be useful to improve the gait and balance issues.

Margaret Mak

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Walking difficulty is one of the cardinal signs leading to disabilities in people with Parkinson's disease (PD). PD patients manifest continuous gait impairment such as reduced stride length, reduced gait speed, and increased stride time variability and/or episodic gait disorders such as freezing of gait, which predispose them to falls. In fact, walking is the most common fall-related activity among PD patients. Physiotherapists play an important role in the rehabilitation of walking which includes both evaluation and treatment. Gait assessment is carried out to understand the biomechanical mechanisms underlying gait disorders so as to design appropriate treatment strategies as well as to evaluate treatment outcomes. Numerous studies have found that the use of external cues results in immediate improvement of stride length, walking speed, and walking pattern. These cues include auditory cues, visual cues, tactile cues, or cognitive cues. There are preliminary reports on the benefits of external cues on enhancing dual cognitive-walking and turning tasks. In addition to cued training, gait training on a treadmill has been found to increase walking speed and reduce variability of gait and freezing of gait. Recent studies reported the effects of non-invasive brain stimulation techniques such as repetitive transcranial magnetic stimulation on enhancing walking performance in PD patients. Research evidence on these approaches and the proposed mechanisms will be presented.

## **The Therapeutic Effect of Hepcidin in Parkinson's Disease Via Regulation of Brain Iron and $\alpha$ -Synuclein Accumulation**

Ya Ke

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Experimental and clinical evidence suggest that abnormal iron accumulation is involved in the pathogenesis of Parkinson's disease (PD). Since the hormone hepcidin is the main regulator of body iron level, including that in the brain, we hypothesise that hepcidin offers therapeutic potential in Parkinsonism. We tested our hypothesis based on a rat model of PD via chronic injection of rotenone. In this model that captures the clinical features of PD with respect to  $\alpha$ -synuclein accumulation as well as the progressive nature of the disorder, we found that chronic rotenone treatment resulted in selective accumulation of  $\alpha$ -synuclein and iron in the substantia nigra pars compacta, which was accompanied by degeneration of dopamine neurons. The motor ability, assessed by the open field test and grid test, was also significantly reduced. Injection of the adenovirus-hepcidin starting on day 5 into the lateral cerebral ventricle could significantly rescue the motor deficit induced by rotenone. Postmortem examination and in-vitro experiments revealed that the over-expressed hepcidin could suppress  $\alpha$ -synuclein and iron accumulation, and reduced neuronal toxicity. Together, these results strongly suggest that manipulating the level of the hepcidin could be a promising therapeutic strategy for PD.

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WH Yung

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High-frequency deep brain stimulation (DBS) applied to the subthalamic nucleus (STN) has proved to be useful in treating Parkinson's disease (PD), but its mechanism remains enigmatic. In principle, DBS can directly activate a wide range of neuronal elements in the target and surrounding areas, including neuronal soma, nerve terminals and axons of passage. We hypothesise that abnormal activities in the primary motor cortex play a critical role in the manifestation of PD symptoms and could be a target of DBS. To enable us to address this question on an animal model of PD, we made recordings of both single-unit activities and local field potentials in the motor cortex of freely moving hemi-Parkinsonian rats before, during, and after STN-DBS. In these movement-disabled animals, abnormal beta rhythm in the motor cortex was found, which was accompanied by marked increase in burst firing and synchrony among layer V motor cortical projection neurons. During the delivery of STN-DBS, we identified short-latency antidromic spikes in layer V neurons. Intriguingly, increased failure rate with increasing stimulation frequency produced the highest number of random antidromic spikes at 125 Hz stimulation, which correlated with the optimal therapeutic efficacy on these animals. This effect was accompanied by increased firing rate, reduced burst spiking and synchrony of firing in the motor cortical neurons. Field potential analysis revealed normalisation of the pathological beta rhythm. Importantly, we found evidence that the firing probability of the cortical projection neuron was modified following the occurrence of an antidromic spike suggesting that direct interference of synchronised firing by stochastic antidromic spikes underlies the beneficial effect. Our results therefore support that STN-DBS antidromically activates output neurons in the motor cortex through the corticosubthalamic nucleus projection, which directly disrupts abnormal neural activities in the motor cortex in PD. Although direct stimulation of the motor cortex in patients is still controversial, our results highlight that given a suitable stimulation paradigm, the motor cortex could be a potential target for the treatment of PD.

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Spinocerebellar ataxias (SCA) 1, 2, 3 and 6 are the most common autosomal dominantly inherited cerebellar degenerations. In the Chinese population, the most common SCA is SCA3 and the frequency of SCA3 among SCA patients is 72.5%, followed by SCA2 with the frequency of 12% among SCA patients. For SCA1, the frequency among SCA patients is 7%. Even though SCAs are rare diseases, a significant number of Chinese in Hong Kong still suffer from this disorder. Hong Kong Spinocerebellar Ataxia Association has 88 members who are suffering from cerebellar degeneration, many of them have a genetic confirmation.

As there are few treatments for SCA, understanding its clinical manifestation and disease mechanisms is the first step towards development of effective treatment. In Europe and North America, two largest SCA consortia involving many medical centres, European SCA group (EUROSCA), and Clinical Research Consortium for Spinocerebellar Ataxias (CRC-SCA) have established bio-repository banks to collect SCA patients' clinical and genetic information as well as the natural history of SCAs. From the natural history studies of SCA1, 2, 3, 6, and 7, of these two consortia, they also developed Scale for the Assessment and Rating of Ataxia (SARA), which is a validated clinical tool to reliably quantify the degree of ataxia symptoms. However, we do not have a centralised ataxia centre collecting such information and specimen in Hong Kong. Establishing an ataxia registry for clinical and genetic information in Hong Kong will facilitate the ataxia research worldwide.

Spinocerebellar ataxias (SCAs) are a group of genetically diverse neurodegenerative disorders causing cerebellar degeneration and progressive ataxia. There are currently 36 types of SCA reported but only 21 disease-causing genes/mutations have been determined. Identifying the underlying mutations enables mechanistic investigation of pathogenesis and subsequent therapeutic development of SCAs. By performing exome and whole-genome sequencing on multiple family members of an autosomal dominant SCA family, we identified a single-point mutation in the coding region of a protein-coding gene in all affected individuals. Further, this mutation was not observed in over 200 control genomes collected in the local population. Clinically, the patients exhibited typical cerebellar ataxia signs and magnetic resonance imaging showed obvious pontocerebellar atrophy along with a global reduction in brain volume. Since no known SCA has previously been assigned to the genetic locus of the identified mutation, our study unveiled a novel form of autosomal dominant type of SCA and we named this condition SCA37.



Ken KL Yung

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Neurodegenerative diseases including Alzheimer's and Parkinson's diseases can cripple lives to varying degrees: from minor disability to loss of movement or memory. At present, there are only limited therapies for neurodegenerative diseases. Research in neural stem cell and regenerative medicine using functional neural stem cells from adult human brain is currently hindered due to risks with brain surgery and the uncertainty in the location of extraction. Herein, we have adopted latest interdisciplinary designs and then combine the novel nanomaterials to develop an innovative treatment. We demonstrate a simple magnetic separation method for the single-step extraction of stem/progenitor cells from choroid plexus lining along the subventricular zone by applying antibodies-conjugated magnetic iron oxide nanoparticles (Ab-MNPs) to the corresponding region in a rat brain with a superfine micro-syringe. It is shown that the magnetically isolated but active stem cells can be developed into neurospheres and differentiated into different types of cells in culture medium in-vitro outside the subject body. This unique characteristic leads us to develop a new tailor-made neurological disorder therapy as the cells can be extracted, modified, and re-applied to the same subject. As the cells are originated from the patients themselves, the risk of immune rejection can be greatly reduced. We believe that this method could be adoptable as a new tailor-made stem cell therapy by harvesting, engineering, and dosing to individual patients' own neural stem cells for neurological treatments.

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## **Identification and Characterisation of a Cognitive Enhancer from Traditional Chinese Medicine**

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Neurodegenerative diseases, characterised by progressive loss of neurons, are emerging to become a major health burden in societies with a large ageing population. Increasing evidence suggests that synaptic dysfunction plays a key role in the onset and progression of neurodegenerative diseases. To this end, we have leveraged our research strengths in molecular neuroscience and Chinese medicine to establish a focused drug discovery programme in search of novel drug leads, including those that can regulate synaptic activity. We report here the discovery of a multivalent herb-derived compound, which modulates function of the AMPA-type of glutamate receptor by increasing serine phosphorylation of AMPA receptor subunit GluA1, which is important for trafficking GluA1-containing AMPA receptors to the synapses. Administration of this compound activates an array of signalling pathways that are critical for synaptic plasticity, resulting in increased protein expression of the neurotrophin brain-derived neurotrophic factor and enhanced level of monoamine neurotransmitters in mouse hippocampus. Furthermore, this compound can rescue impaired long-term potentiation in brain slices either treated with amyloid-beta oligomers or isolated from Tg2576 Alzheimer's disease mouse. In vivo, this compound enhances the reference memory of mice in the Morris water maze task, reduces the duration of immobility in the forced swim test, and rescues neurological deficits in a stroke model. These observations suggest that this compound is an attractive candidate for development as a cognitive enhancer to alleviate memory dysfunctions associated with ageing and neurodegenerative diseases.

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Treatment with interferon-beta or glatiramer acetate has been in routine use for the treatment of clinically isolated syndromes and relapsing-remitting multiple sclerosis (RRMS) for almost two decades. Although many patients remain clinically and radiologically stable on treatment, other patients have either radiological evidence of ongoing disease activity, continue to have relapses, or develop a progressive disease course. Whether such patients should be considered non-responsive, ie refractory to treatment, or to merely have an insufficient response remains a matter of debate.

Some of the emerging oral therapies, eg dimethylfumarate, laquinimod and teriflunomide have been compared to the well-known, injectable first-line therapies in randomised controlled trials without clear evidence of significant differences in clinical efficacy.

For patients with high disease activity treatment immunosuppression with mitoxantrone or cyclophosphamide has been used in some countries, and may still be an option for patients converting to a secondary progressive disease course, although toxicity limits the general use of these treatments. Natalizumab is widely used as a second-line treatment for RRMS, but has never been compared to other treatments in phase 3 trials. Fingolimod treatment was superior to interferon-beta 1a in one clinical trial. In some countries fingolimod is licensed as a first-line therapy, in other countries only for patients with high disease activity or as a second-line therapy. Most recently, lymphocyte depletion with alemtuzumab was shown to be superior to interferon beta-1 both as first-line and second-line therapy.

The choice of treatment for the individual patient with an insufficient treatment response will depend on a thorough evaluation of the previous disease course, treatment history, the presence of risk factors for severe side-effects of therapy, and the evidence of efficacy for the treatment options considered.

## Intracranial Abscesses and Infections of Neurosurgical Shunts and Drains

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An overview of management of intracranial suppurative infection and cerebrospinal fluid (CSF) shunt catheter infection is presented.

Intracranial suppurative infections are life-threatening but eminently treatable conditions. Lacking the alertness of such condition can lead to delay in diagnosis and treatment. The clinical features, imaging finding, role of surgery, and antibiotics treatment strategies in the management of intracranial suppurative infection are discussed. With the increasing popularity of endovascular intervention, we are seeing more and more intracranial infective complications related to indwelling devices and intra-arterial administration of medication. Illustrative cases are presented.

The second part of the presentation is related to CSF shunt catheter infection. Although CSF shunting has been remarked as the most successful invention in the history of neurosurgery, neurosurgeons are trying hard to avoid putting in shunts in their patients nowadays. Shunt catheter infection is the most common complication in CSF shunting operation. Aetiological factors, ways to avoid catheter infection, diagnosis, and management of shunt infection are discussed. Indications of prophylactic antibiotics for patients with CSF shunt going for dental procedures, gastrostomy, and laparotomy are discussed.

## The 'Not So Common' Causes of Central Nervous System Infection in Hong Kong: Diagnoses You Cannot Afford to Miss

S 15

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Infection of the central nervous system is an infectious disease emergency frequently encountered by the neurologists in clinical practice. Early diagnosis and treatment is essential in reducing the significant morbidity and mortality associated with these infections. Unfortunately, up to two thirds of encephalitis cases and a large number of chronic or partially treated acute meningitis cases remain of unknown aetiology despite an extensive diagnostic workup. In a metropolitan city with a high standard of health care like Hong Kong, most physicians are competent in managing patients with central nervous system infections caused by common pathogens with established diagnostic algorithms and treatment strategies. However, cases caused by unusual pathogens or those with atypical manifestations often cause diagnostic dilemmas, and hence, delay in treatment. An individualised clinical management approach with a specific focus on epidemiological risk assessment and close liaison with the clinical microbiology laboratory for state-of-the-art diagnostic tests are essential in deciphering the secrets of infections caused by these 'not so common' bugs.

## Ten Minutes Vestibular Examinations but Persistent Rehabilitative Exercises

S 16

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Vertigo is a common illness that patients seek consultation in ENT clinics. Patients often have a hallucination of environmental rotation while patients with dizziness often have a sense of light-headedness. This presentation will introduce some useful but succinct clinical examinations that medical practitioners can do in about 10 minutes to make initial diagnosis whether the vertigo has a peripheral or central cause before referring the patient for more sophisticated vertigo and vestibular assessments. Some latest technologies in assessing vestibular functions are also introduced. Vestibular or dizzy rehabilitative exercise should follow if permanent vestibular paresis is found. With unilateral vestibular lesions, asymmetry of tonic vestibulospinal activity may lead to postural and gait imbalance. With symmetrical vestibular loss, the imbalance will be more pronounced and persistent. This presentation introduces some vestibular or dizziness exercises that can be practised by the patients at home. These exercises try to provoke imbalance and dizziness but at the same time try to improve the brain to compensate for any abnormalities in the vestibular system and to retrain the brain to adapt and tolerate the information from the deficit vestibular apparatus. The exercises also train the visual and somatosensory systems to compensate and assist in balancing and reduce the sense of dizziness.

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Primary headaches are common neurological problems and are a socioeconomic burden. The quality of life can be severely jeopardised if the pain is not adequately controlled. The chronic forms, chronic daily headache, are the most disabling and are usually refractory to medications. Primary chronic daily headaches can be due to chronic tension-type headache (CTTH), chronic migraine (CM), new daily persistent headache (NDPH), chronic cluster headache (CCH), chronic paroxysmal hemicrania (CPH), short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), short-lasting unilateral neuralgiform headache attacks with autonomic symptoms (SUNA) and hemicrania continua (HC).

Neurostimulation is recently emerging as a novel treatment modality for patients with chronic, disabling, and drug-refractory primary headache disorders. Central neurostimulation methods include deep-brain stimulation (DBS) and transcranial magnetic stimulation (TMS) whereas peripheral neurostimulation modalities include occipital nerve stimulation (ONS), vagus nerve stimulation (VNS), sphenopalatine ganglion stimulation (SPS), auriculotemporal nerve stimulation and supraorbital nerve stimulation. The preliminary results of DBS and ONS are promising. Currently there are more than 60 patients with drug-resistant cluster headache (CH) implanted with DBS with 64% success rate in pain reduction. The rationale of DBS in CH stems from the finding of hyperactivation of posterior hypothalamus in the functional imaging during headache attack. For ONS, its efficacy in treating headache pain was first observed from its successful treatment in drug-resistant occipital neuralgia and so far there are about 500 CM and 90 CH patients treated by ONS with pain improvement rate of 56% and 67%, respectively. In the ongoing randomised controlled trial, the ONSTIM trial, the preliminary results suggest that ONS is more effective than placebo or medical therapy in medically intractable chronic migraine.

In summary, ONS and DBS of posterior hypothalamus seem to be effective in CCH, and ONS seems to be a promising treatment in CM. More data from further randomised controlled trial are needed to confirm their efficacy.

**Late-onset Pompe Disease in the New Enzyme Replacement Therapy Era**

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Pompe disease (PD) is an autosomal recessive disorder caused by the deficiency of lysosomal enzyme acid  $\alpha$ -glucosidase (GAA). The disease has two clinical forms. The classic infantile form develops severe hypotonia and hypertrophic cardiomyopathy shortly after birth. Until enzyme replacement therapy (ERT) becomes available, victims of this devastating form seldom survive beyond their second birthday. Late-onset PD (LOPD) is more heterogeneous. Patients usually present with a limb girdle pattern of muscle weakness and develop respiratory impairment early on, but the heart is almost always spared. The clinical form and severity of the phenotype is correlated to the amount of residue GAA activity, which is determined by the mutations. In a compound heterozygous mutation, if one allele carries a severe mutation, eg frame shift, the resulted phenotype will be a severe one. Unfortunately, the common mutation in Chinese is a severe one; our LOPD patients often have severe phenotype, with earlier symptom presentation, respiratory failure, and requirement of assisted ventilation. ERT with  $\alpha$ -glucosidase- $\alpha$  (myozyme) was first licensed by Food and Drug Administration in 2006 for treatment of infantile PD, and the drug was available in Hong Kong since 2008. Following the publication on the first randomised trial of myozyme in LOPD in 2010, Hong Kong started the first ERT on two brothers in December 2010. There are now five LOPD patients on ERT. Four patients had ERT for more than 1 year, all showed improvement or stabilisation of their respiratory function and mobility, the overall response was comparable or even better than that in the clinical trials. Nevertheless, these patients have an aggressive phenotype; their clinical course is different from the subjects in clinical trials. It is still too early to conclude whether these early benefits could be sustainable over time. ERT not only brings the first effective treatment in LOPD, it also magnifies the benefit of adjuvant therapies including nutrition and exercise, which only provide transient or short-term effects in the pre-ERT era. New strategies to improve the efficacy of ERT is on-going; better tissue delivery, autophagy targeted, biologic chaperones, and the use of  $\beta_2$  agonist albuterol to boost the lean muscle are among the many fancy ideas. Many questions await answers and many problems are unsettled, but a better future is promised in LOPD.

## Experience of Using Intravenous Thrombolysis in Elderly Patients with Major Acute Ischaemic Stroke in Kwong Wah Hospital

P 1

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Elderly patients with major ischaemic strokes may remain severely handicapped or dead. We reported two elderly patients aged greater than 80 years at the time of intravenous thrombolysis treatment given in 2009 to 2010.

An 84-year-old man (patient 1) with a history of paroxysmal atrial fibrillation was admitted to Kwong Wah Hospital in March 2010 for congestive heart failure. He developed acute right hemiplegia during hospitalisation with NIHSS 26. Urgent computed tomography (CT) of the brain was unremarkable. Intravenous thrombolysis was commenced after evaluation. Follow-up NIHSS 1 day later was 13. CT following the next day revealed an infarct in anterior part of left middle cerebral artery territory. There was no sign of haemorrhagic transformation. Stroke risk factors were being optimised. He was able to walk with stick under supervision with residual expressive dysphasia after a course of rehabilitation. Improvement of Barthel Index (BI) from 0 to 79 was reported after 3 months of training.

Another 83-year-old woman (patient 2) was able to walk unaided prior to admission. She had a history of hypertension and was admitted in year 2009 for hyperacute stroke presented with dense right hemiplegia upon admission with NIHSS 15. Urgent CT of brain was unremarkable. She was treated with intravenous thrombolysis with good neurological recovery. The patient was discharged to rehabilitative care on day 8. At 3-month follow-up, she was able to walk with stick with good achievement in BI score from 48 to 90 after rehabilitation.

Acute thrombolysis therapy is an effective treatment for acute ischaemic stroke. However, elderly patients have mostly been excluded from acute revascularisation trials, due to poor prognosis as a result of concurrent medical illness, and fear of haemorrhagic events from these treatment.

The above two cases showed that thrombolysis benefits elderly stroke patients. Improvement in BI was contemplated in these two patients. In carefully selected patients who meet eligibility criteria for thrombolysis, treatment should not be withheld on the basis of age alone.

## Griffiths Mental Developmental Scales Validation for Chinese Children

P 2

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**Background:** The Griffiths Mental Developmental Scales (GMDS) have been used extensively by doctors and psychologists in many countries to assess a child's developmental profile. In China, there is an increasing awareness of developmental disorders in children; the prevalence of preschool children with developmental disorders was reported to be as high as 12.97%. The GMDS have been devised based on observation of the performance of children living in the West. However, there are obvious differences in the culture and beliefs of people growing up in Asia as compared to those living in western societies. In this study, the GMDS have been translated into Chinese and modified according to Chinese culture. This prospective study aimed to provide validation of the GMDS for Chinese children.

**Methods:** Chinese children from seven different cities in China with apparently normal development with no significant medical history were recruited into the study. Their developments were assessed using the GMDS.

**Results:** GMDS scores were collected and analysed for a total of 815 Chinese children with ages ranging from 1 month to 8 years old; 391 (48%) were female. Smooth 'developmental growth' charts and standard deviation/percentile scores were computed for each of the neurological developmental scales using the LMS method. Plots of the 1st, 2.5th, 5th, 10th, 25th, 50th, 75th, 90th, 95th, 97.5th, and 99th percentiles will be presented for each of the six sub-scales and the overall Griffiths score.

**Conclusion:** There are differences in the Chinese developmental percentile curves as compared to the British developmental percentile curves. These differences are most obvious in subscale F. Chinese children should be assessed using our validated Chinese 'developmental growth' charts. This will prevent under-estimating or over-estimating the developmental milestones in Chinese children.

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**Background and purpose:** Seizure is an important co-morbidity of stroke. This study investigated the characteristics/prognosis of patients with acute symptomatic seizure (AS) (early, <7 days of stroke) after ischaemic stroke (IS). These outcome measures are important when considering controversial treatment options in patients with concurrent IS/AS.

**Methods:** We prospectively investigated 2925 IS patients from a population-based acute stroke unit (ASU). The stroke-related parameters were age/sex, stroke aetiology, stroke severity, functional disability, transient-complete occlusion, or partial recanalisation, multiple-territory infarct and haemorrhagic transformation. The seizure-related parameters were (1) AS co-occurring with incident IS (CS, day 2-7 after stroke), (2) AS following the recurrence of IS (ASS >7 days after incident stroke with another IS/AS), (3) remote symptomatic seizure (US, >7 days after incident stroke without IS). We excluded patients with intracerebral haemorrhage, subdural haematoma, subarachnoid haemorrhage, or venous infarcts.

**Results:** The incidence of AS in IS was 3.9% (115/2925). A total of 104 patients with AS/IS (mean age, 65 years; 55% female) had a mean National Institute of Stroke Scale (NIHSS) score of 11. Cardio-embolism was found in 48.1% (50/104) and transient-complete occlusion/partial recanalisation in 30.8% (32/104). Haemorrhagic transformation was only found in 16.4% (17/104). The combined risk of CS+ASS was 28% at 1 year, 30% at 2 years and 40% at 8 years. The risk of developing US was 28% at 8 years. Status epilepticus, presence of another acute symptomatic cause, >2 cardiovascular risk factors were predictive of CS+ASS ( $P<0.05$ ) and epileptiform discharge on electroencephalogram (EEG) for US ( $P=0.04$ ). Subgroup analysis of AS/IS with seizure-at-onset did not differ in their characteristics or prognostic indicators.

**Conclusions:** While the long-term risk of developing epilepsy after IS/AS was only 28%, additional acute symptomatic seizures are found with index stroke or during recurrent strokes in another 40%. This has implications for short-to-medium term antiepileptic drug treatment. The prognosis in terms of haemorrhagic transformation in patients presenting with ischaemic stroke and seizure at onset without thrombolysis being given was 16%.

<b>AUTHOR INDEX</b>		Page No.
<b>A</b>		Page No.
LI Ao	28	
DKK Au	26	
<b>C</b>		
D Challis	28	
AYY Chan	23	
EHY Chan	23	
GHF Chan	20	
JFW Chan	26	
RCK Chan	27	
TY Chan	28	
ZY Chen	19	
PW Cheng	17	
WK Cheng	11, 28	
<b>D</b>		
KX Du	28	
<b>F</b>		
YW Fan	25	
MK Fong	14	
CW Fung	13	
ELW Fung	20	
<b>H</b>		
ACC Ho	13	
LF Hui	10	
<b>I</b>		
FCF Ip	24	
MF Ip	12	
NY Ip	24	
<b>J</b>		
FY Jiao	28	
<b>K</b>		
Y Ke		21
KF Ko		11, 28
MC Kwan		11, 28
CM Kwok		10
AKY Kwong		13
<b>L</b>		
ML Lai		28
WY Lau		11, 28
C Leung		29
EYC Leung		16
H Leung		29
T Leung		29
M Li		28
SH Li		12
HT Lui		10
WM Lui		18
<b>M</b>		
KK Ma		12, 15
M Mak		21
V Mok		29
<b>S</b>		
F Sellebjerg		25
B Sheng		27
Y Soo		29
<b>T</b>		
WWY Tso		28
<b>W</b>		
TY Wai		12
AHY Wong		14
KS Wong		29

---

	Page No.
KY Wong	10
PTY Wong	9
VCN Wong	9, 13, 28
<b>X</b>	
XL Xia	28
X Xu	28
<b>Y</b>	
PYP Yau	20
H Yip	11, 28
KKL Yung	24
WH Yung	22
<b>Z</b>	
X Zhang	28
LM Zhou	19



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