HONG KONG MEDICAL JOURNAL 香港醫學雜誌
SUPPLEMENT 7
VOLUME 15 ▪ NUMBER 6 ▪ DECEMBER 2009

1st Hong Kong Neurological Congress cum 22nd Annual Scientific Meeting of the Hong Kong Neurological Society
6–8 November 2009

Council of the Hong Kong Neurological Society 5

Organising Committee 5

List of Speakers 6

Scientific Programme 7

SESSION	ABSTRACT	PAGE
SYMPOSIUM ON MOVEMENT DISORDERS **Joint Symposium with the Hong Kong Movement Disorder Society and Hong Kong Baptist University (supported by Croucher Foundation)**		
Neurodegeneration: the Processes *Raymond CC Chang, Jianfei Chao, Yuen-shan Ho, Mingfu Wang*	**S1**	11
Genetics in Parkinson's Disease: Any Emerging Picture? *Yoshikuni Mizuno*	**S2**	12
Therapeutic Implications of Modulations of Glutamatergic Neurotransmission in Models of Parkinson's Disease *Ken KL Yung*	**S3**	13
Neuronal Mitochondrial Uncoupling Proteins: Implications in Parkinson's Disease *Philip Ho*	**S4**	13
Glial Pathologies in Parkinsonism *Glenda Halliday*	**S5**	14
Managing Different Stages in Parkinson's Disease: an Update *Yoshikuni Mizuno*	**S6**	15
Non-dopaminergic Degeneration in Motor Circuits and Their Impact on the Treatment of Parkinson's Disease *Glenda Halliday*	**S7**	16
SYMPOSIUM ON STROKE **Joint Symposium with the Hong Kong Stroke Society**		
Central Post-stroke Pain *Jong-sung Kim*	**S8**	17
Optimising Delivery and Outcome in Stroke Thrombolysis—Experience from Singapore *Bernard Chan*	**S9**	17
Acute Stroke Care in Singapore *Bernard Chan*	**S10**	18
A Retrospective Review of Endovascular Treatment of Cerebral Aneurysm in Hong Kong *John CK Kwok, KM Cheng, WM Lui, KY Pang, CB Tan, Simon Yu*	**S11**	18

SESSION	ABSTRACT	PAGE
Current Neurovascular Practice in Sydney, 2009 *Bernard Kwok*	**S12**	19
GSK—SYMPOSIUM ON EPILEPSY I **Joint Symposium with Hong Kong Epilepsy Society**		
Status Epilepticus in 2009: What We Know and What We Don't *David Treiman*	**S13**	20
Pharmacogenomics of Epilepsy: an Update *Patrick Kwan*	**S14**	22
SYMPOSIUM ON EPILEPSY II **Joint Symposium with Hong Kong Epilepsy Society**		
Neuropsychological Outcome Following Anterior Temporal Lobectomy for Epilepsy *Iris Chan*	**S15**	22
Reflex Seizures *Shang-yeong Kwan*	**S16**	23
Women with Epilepsy: Preconception, Pregnancy and Post-delivery Care *Terence J O'Brien*	**S17**	23
Merck Pharmaceutical (HK)—SYMPOSIUM ON MULTIPLE SCLEROSIS		
Optimising Treatment Outcome for Multiple Sclerosis *Kwok-kwong Lau*	**S18**	24
Evidence-based Medicine for Long-term Multiple Sclerosis Treatment (PRISMS LTFU) *Douglas S Goodin*	**S19**	24
SYMPOSIUM ON NEUROMUSCULAR DISORDERS		
Pattern Recognition Approach to Muscle and Neuromuscular Junction Disorders *Richard J Barohn*	**S20**	25
How to Get the Best Out of Your Pathology Laboratory in Neuromuscular Diseases? *Ho-keung Ng*	**S21**	26
Treatment and Clinical Research in Myasthenia Gravis: How Far Have We Come? *Richard J Barohn*	**S22**	26
FREE PAPER PRESENTATIONS		
Expedited Stroke Triage Pathway is Key to Shorten Door-to-needle Time in Delivery of Thrombolysis Treatment *Alexander YL Lau, Thomas Leung, Yannie OY Soo, Eddie Wong, Anne YY Chan, Lisa Au, Vincent Ip, Cecilia Leung, Venus Hui, Wai-ching Shum, Lawrence KS Wong*	**FP1**	27
The Application of Wavelet Technology in the Interpretation of Scalp Electroencephalogram *Howan Leung, Anne YY Chan, Alexander YL Lau, Ka-lau Leung, Cannon XL Zhu, Danny TM Chan, Patrick Kwan, Lawrence KS Wong*	**FP2**	28
Double-blind Randomized Control Trial of Acupuncture for Autistic Spectrum Disorder *VCN Wong, WX Chen, WL Liu*	**FP3**	29

SESSION	ABSTRACT	PAGE
Evaluation of Perfusion Computed Tomography in Patients with Multiple Large Artery Atherosclerosis *Yannie OY Soo, Thomas Leung, Henry Mak, Simon Yu, Wynnie Lam, Lawrence KS Wong*	**FP4**	29
Clinical Utility of National Institutes of Health Stroke Scale (NIHSS) in Screening Patients with Acute Stroke for Receiving Recombinant Tissue–Plasminogen Activator *May YN Mok, Sonny FK Hon, Richard Li, CN Lee, Eric SW Yeung, M AuYeung, CM Cheung, TH Tsoi*	**FP5**	30
Autonomic Dysfunction on Functional Outcome After Acute Ischaemic Stroke *JL Xiong, Howan Leung, XY Chen, JH Han, Thomas Leung, Yannie OY Soo, Edward Wong, Anne YY Chan, Alexander YL Lau, Lawrence KS Wong*	**FP6**	30
Ketogenic Diet Programme for Children with Intractable Epilepsy in the Hong Kong West Cluster—13-Year Experience *Ada WY Yung, Virginia CN Wong*	**FP7**	31
A Study of Cerebrospinal Fluid Neurotransmitters Assay in Children with Undiagnosed Neurological Diseases in Hong Kong *CW Fung, S Siu, G Poon, A Kwok, PT Cheung, L Low, C Mak, S Tam, VCN Wong*	**FP8**	32
DISSERTATION HIGHLIGHTS		
Prediction of Spontaneous Haemorrhagic Transformation of Acute Major Cerebral Infarcts by Magnetic Resonance Imaging with Susceptibility-weighted Imaging Sequence *Hiu-fai Chan*	**D1**	33
A Study on Anticoagulant Prescription after Acute Stroke in Non-valvular Atrial Fibrillation Patients in the Chinese Community *Cynthia Chen*	**D2**	34
Valvular Heart Disease and Use of Bromocriptine in Patients with Parkinson's Disease *Chun-pong Chung*	**D3**	35
Utility of Specific Cerebral Angiographic Features in Distinguishing Reversible Cerebral Vasoconstriction Syndromes from Primary Angiitis of the Central Nervous System *Joshua W Fok*	**D4**	36
BAD: the Missing Link *May WM Kwan*	**D5**	37
Clinically Isolated Syndrome in Hong Kong and Long-term Outcomes *Richard Li*	**D6**	37
Aspirin Failure in Non-cardioembolic Ischaemic Stroke: a Retrospective Cohort Study on Its Incidence, Choice of Antiplatelet Treatment, and Clinical Outcome *Alan CT Tse*	**D7**	38
POSTERS		
Central Nervous System Lymphoma—Clinical, CT and MR Correlation *KY Lau, EMW Man, WWC Wong, SSW Lo, JLS Khoo, JKW Chan, TH Tsoi*	**P1**	39

SESSION	ABSTRACT	PAGE
Pilot Project of Integration of Chinese Medicine (Acupuncture) and Western Medicine for Neurohabilitation of Children with Acquired Brain Injury—a Study of Two Cases *Virginia CN Wong, L Li, SS Lam, CL Wong, Vanessa Chu; Neurohabilitation Team of Duchess of Kent Children Habilitation Institute*	**P2**	39
Reasons for A&E Consultation and Hospital Admission for Parkinson's Disease *HF Chan, YF Cheung, WC Fong, KW Fong, LT Chan, YC Chan, WT Lo, HF Ho, HM Chan, CK Li*	**P3**	40
Median-ulnar Mixed Nerve Latency Difference to the Mid-palm in Carpal Tunnel Syndrome *Kwai-fu Ko, Kwai-ping Yiu, Wing-yan Lau, Wing-keung Cheng, Min-chung Kwan, Tsz-pang Chan*	**P4**	40
Diffusion-weighted MR imaging of Creutzfeldt-Jakob Disease *R Lee, HK Chan, SYY Pang, SFK Hon, W Mak, RTF Cheung, SL Ho, KS Tai*	**P5**	41
Paediatric Epilepsy Surgery Programme in Hong Kong—Experience in Queen Mary Hospital/Duchess of Kent Children's Hospital *Ada WY Yung, Virginia CN Wong, Pek L Khong, Henry Mak, KN Hung, PH Chan, WY Ho, YW Fan*	**P6**	41
Risk Factors Associated with Refractory Epilepsy in Children—The University of Hong Kong Experience *Virginia CN Wong, Ada WY Yung*	**P7**	42
Posterior Reversible Encephalopathy Syndrome: Paediatric Heart Transplant with Cyclosporine Neurotoxicity *W Tso, AWY Yung, KS Lun, TC Yung, K Fan, VCN Wong*	**P8**	42
Electro-acupuncture for Children with Autism Spectrum Disorder: Pilot Study of Two Cases *WX Chen, WL Liu, VCN Wong*	**P9**	43
Acupuncture for Autistic Spectrum Disorder *DKL Cheuk, VCN Wong, WX Chen*	**P10**	44
Calcium Channel Blockers Can Reduce Iron-induced Apoptosis in Neural Stem Cells *WX Chen, VCN Wong, M Yang, GCF Chan*	**P11**	45
Clinical Course of Patients with Myasthenia Gravis in Hong Kong *Eric SW Yeung, Chi-nam Lee, Richard Li, Sonny FK Hon, M Au-yeung, CM Cheung, TH Tsoi*	**P12**	45
A Girl with Atypical Chronic Inflammatory Demyelinating Polyneuropathy *Sophelia HS Chan, Windsor Mak, Virginia CN Wong*	**P13**	46
Anti-NMDA-R Encephalitis—an Encephalitis Lethargica-like Illness *Sophelia HS Chan, CW Fung, Ada WY Yung, SL Lee, Virginia CN Wong, Russell C Dale, Angela Vincent*	**P14**	47
Suspected Herpes Simplex Encephalitis in a Regional Hospital *MWM Kwan*	**P15**	48
Author Index		50

Council of the Hong Kong Neurological Society

President	Dr Ping-wing Ng 吳炳榮醫生
Vice-President	Dr Leonard Sheung-wai Li 李常威醫生
Hon Secretary	Dr Wing-chi Fong 方榮志醫生
Hon Treasurer	Dr Jonas Hon-ming Yeung 楊漢明醫生
Council Members	Dr Nelson Yuk-fai Cheung 張煜暉醫生
	Dr Sonny Fong-kwong Hon 韓方光醫生
	Dr Kwok-fai Hui 許國輝醫生
	Dr Kwok-kwong Lau 劉國光醫生
	Dr Thomas Wai-hong Leung 梁慧康醫生
	Dr Terrance Ho-lun Li 李可倫醫生
	Dr Colin Hiu-tung Lui 呂曉東醫生
	Prof Vincent Chung-tong Mok 莫仲棠教授
	Dr Kin-lun Tsang 曾建倫醫生
	Dr Winnie Wing-yin Wong 黃詠妍醫生
Past President	Dr Tak-hong Tsoi 蔡德康醫生
Hon Legal Advisor	Mr Tsang-hoi Koo 顧增海律師
Hon Auditor	Mr Eric Li 李家祥先生

Organising Committee of the 1st Hong Kong Neurological Congress cum the 22nd Annual Scientific Meeting of the Hong Kong Neurological Society

Chairman	Dr Ping-wing Ng 吳炳榮醫生
Vice-Chairman	Dr Leonard Sheung-wai Li 李常威醫生
Hon Secretary	Dr Wing-chi Fong 方榮志醫生
Hon Treasurer	Dr Jonas Hon-ming Yeung 楊漢明醫生
Scientific Committee	Dr Nelson Yuk-fai Cheung 張煜暉醫生
	Dr Sonny Fong-kwong Hon 韓方光醫生
	Dr Kwok-fai Hui 許國輝醫生
	Dr Thomas Wai-hong Leung 梁慧康醫生
	Dr Colin Hiu-tung Lui 呂曉東醫生
	Prof Vincent Chung-tong Mok 莫仲棠教授
Publication Committee	Dr Kwok-kwong Lau 劉國光醫生
	Dr Terrance Ho-lun Li 李可倫醫生
	Dr Winnie Wing-yin Wong 黃詠妍醫生
	Dr Tak-hong Tsoi 蔡德康醫生
Website	Dr Kin-lun Tsang 曾建倫醫生

List of Speakers

Name	Affiliations
Dr Richard J Barohn	University of Kansas Medical Center, United States
Prof Terrence O'Brien	The University of Melbourne, Australia
Dr Bernard Chan	The National University Hospital, Singapore
Ms. Iris Chan	Queen Elizabeth Hospital, Hong Kong
Dr John HM Chan	Hong Kong Movement Disorder Society
Prof Raymond Chang	The University of Hong Kong, Hong Kong
Prof Kenny Chung	Hong Kong University of Science and Technology, Hong Kong
Prof Douglas S Goodin	The University of California-San Francisco, United States
Prof Glenda Halliday	University of Sydney, Australia
Prof Philip Ho	The University of Hong Kong, Hong Kong
Prof Yi-ning Huang	Peking Union Medical College Hospital, Beijing, China
Prof Jong-sung Kim	University of Ulsan, Seoul, Korea
Dr Patrick Kwan	Prince of Wales Hospital, Hong Kong
Dr Shang-yeong Kwan	National Yang-Ming Medical College, Taiwan
Dr Bernard Kwok	Prince of Wales Private Hospital, Sydney, Australia
Dr John Kwok	Kwong Wah Hospital, Hong Kong
Dr Kwok-kwong Lau	Princess Margaret Hospital, Hong Kong
Dr Shih-hui Lim	National Neuroscience Institute, Singapore
Prof Yoshikuni Mizuno	Jutendo University, Tokyo, Japan
Prof Ho-keung Ng	The Chinese University of Hong Kong, Hong Kong
Dr Ping-wing Ng	The Hong Kong Neurological Society
Prof C Warren Olanow	Mount Sinai School of Medicine, New York
Prof Chong-tin Tan	University of Malaya, Malaysia
Prof David M Treiman	Barrow Neurological Institute, United States
Prof Lawrence KS Wong	The Chinese University of Hong Kong, Hong Kong
Dr Ada Yung	Queen Mary Hospital, Hong Kong
Prof Ken KL Yung	Hong Kong Baptist University, Hong Kong

SCIENTIFIC PROGRAMME

Venue: Kowloon Shangri-La Hotel

6 November 2009, Friday

09:00 – 09:30 Registration

09:00 – 11:15 **SYMPOSIUM ON MOVEMENT DISORDERS**

Joint Symposium with the Hong Kong Movement Disorder Society and Hong Kong Baptist University (supported by Croucher Foundation)
SESSION 1: Basic Science in Movement Disorders

Chairpersons: *Ken Yung, Jonas Yeung*

Opening Remarks
John Chan, President, Hong Kong Movement Disorder Society
Ken Yung, Professor, Department of Biology, Hong Kong Baptist University

Neurodegeneration: the Processes
Raymond CC Chang

Genetics and Mechanisms in Parkinson's Disease
Kenny Chung

Genetics in Parkinson's Disease: Any Emerging Picture?
Yoshikuni Mizuno

Parkinson's Disease and Prion Disease
C Warren Olanow

11:15 – 11:35 Coffee Break

11:35 – 13:00 **SYMPOSIUM ON MOVEMENT DISORDERS**

Joint Symposium with the Hong Kong Movement Disorder Society and Hong Kong Baptist University (supported by Croucher Foundation)
SESSION 1: Basic Science in Movement Disorders (Cont'd)

Chairpersons: *WH Yung, Nelson Cheung*

Therapeutic Implications of Modulations of Glutamatergic Neurotransmission in Models of Parkinson's Disease
Ken KL Yung

Neuronal Mitochondrial Uncoupling Proteins: Implications in Parkinson's Disease
Philip Ho

Glial Pathologies in Parkinsonism
Glenda Halliday

13:00 – 14:00 Lunch/Press Conference

14:00 – 15:30 **SYMPOSIUM ON MOVEMENT DISORDERS**

Joint Symposium with the Hong Kong Movement Disorder Society and Hong Kong Baptist University (supported by Croucher Foundation)
SESSION 2: Clinical Practice in Movement Disorders

Chairpersons: *John Chan, PW Ng*

Managing Different Stages in Parkinson's Disease: an Update
Yoshikuni Mizuno

Neuroprotection
C Warren Olanow

15:30 – 15:45 Coffee Break

15:45 – 17:00

SYMPOSIUM ON MOVEMENT DISORDERS

Joint Symposium with the Hong Kong Movement Disorder Society and Hong Kong Baptist University (supported by Croucher Foundation)
SESSION 2: Clinical Practice in Movement Disorders (Cont'd)

Chairpersons: *Vincent Mok, Xian-Lun Zhu*

Non-dopaminergic Degeneration in Motor Circuits and Their Impact on the Treatment of Parkinson's Disease
Glenda Halliday

Future Directions in Movement Disorders Researches: New Thinking and Paradigms
Open discussion

Concluding Remarks
John Chan, PW Ng, Ken Yung

7 November 2009, Saturday

09:00 – 09:30 Registration

09:00 – 10:00

Grand Ballroom

Hong Kong Epilepsy Society Workshops
Chairpersons: *Dawson Fong, Patrick Kwan*

Classification of Seizures
Chong-tin Tan

Status Epilepticus: an Electro-clinical Approach to Diagnosis and Classification
David Treiman

Function Room
09:00 – 10:20
Free Paper Presentation
Chairpersons:
Jonas Yeung, WC Fong

10:00 – 10:30 Coffee Break

10:30 – 12:30

Grand Ballroom

Hong Kong Epilepsy Society Workshops
Chairpersons: *Dawson Fong, Patrick Kwan*

Is it Epileptic Seizure?
SH Lim

Quiz: "Ask the audience"
Chong-tin Tan, David Treiman, SH Lim

"Ask the experts"
Local speakers

Function Room
10:30 – 12:30
Dissertation Highlights
Chairpersons:
PW Ng, Thomas Leung

12:30 – 14:00 Lunch/Press conference

Sanofi-BMS – Lunch Symposium
Chairperson: *TH Tsoi*

Update of Antithrombotic Therapy in the Prevention of Stroke in Atrial Fibrillation Patients
Lawrence KS Wong

14:00 – 14:10	Grand Ballroom **OPENING CEREMONY** Welcome remarks: *PW Ng*, President, The Hong Kong Neurological Society Guest of Honour: *Dr Hon Ka-lau Leung*	Function Room 14:00 – 17:00 **ASEPA EEG EXAM PART 2** Examiners: *SH Lim* *CT Tan* *SY Kwan* *T O'Brien*
14:10 – 15:40	**SYMPOSIUM ON STROKE** **Joint Symposium with the Hong Kong Stroke Society** **SESSION 1: Medical Issues in Stroke Management** Chairpersons: *Raymond TF Cheung, CY Huang* **Central Post-stroke Pain** *Jong-sung Kim* **Recent Epidemiology Studies on Intracranial Atherosclerosis in China** *Yi-ning Huang* **Optimising Delivery and Outcome in Stroke Thrombolysis—Experience from Singapore** *Bernard Chan* **SESSION 2: Acute Stroke Care Forum** **Acute Stroke Care in Korea** *Jong-sung Kim* **Acute Stroke Care in Mainland China** *Yi-ning Huang* **Acute Stroke Care in Singapore** *Bernard Chan* **Open Forum**	
15:40 – 16:00	Coffee and Tea Break	
16:00 – 17:00	Grand Ballroom **SYMPOSIUM ON STROKE** **Joint Symposium with the Hong Kong Stroke Society** **SESSION 3: Surgical Issues and Endovascular Interventions in Stroke Management Review** Chairpersons: *Richard Kay, Dawson Fong* **A Retrospective Review of Endovascular Treatment of Cerebral Aneurysm in Hong Kong** *John CK Kwok* **Current Neurovascular Practice in Sydney, 2009** *Bernard Kwok*	
Evening	Faculty Dinner	

8 November 2009, Sunday

09:00 – 09:30 Registration

09:15 – 10:40 **GSK – SYMPOSIUM ON EPILEPSY I**

Joint Symposium with Hong Kong Epilepsy Society

Chairpersons: *Jason Fong, Terrance Li*

Status Epilepticus in 2009: What We Know and What We Don't
David Treiman

Genetics of Paediatric Epilepsy Syndromes
Ada Yung

Pharmacogenomics of Epilepsy: an Update
Patrick Kwan

10:40 -11:00 Coffee Break

11:00 – 12:30 **SYMPOSIUM ON EPILEPSY II**

Joint Symposium with Hong Kong Epilepsy Society

Chairpersons: *Colin Lui, Bell Tse*

Neuropsychological Outcome Following Anterior Temporal Lobectomy for Epilepsy
Iris Chan

Reflex Seizures
Shang-yeong Kwan

Women with Epilepsy: Preconception, Pregnancy and Post-delivery Care
Terrence J O'Brien

Function Room
09:00 – 12:30
POSTER PRESENTATION

12:30-14:00 Lunch/Press Conference

14:00 – 15:00 **MERCK PHARMACEUTICAL (HK) - SYMPOSIUM ON MULTIPLE SCLEROSIS**

Chairpersons: *Patrick Li, Edmund Woo*

Optimising Treatment Outcome for Multiple Sclerosis
Kwok-kwong Lau

Evidence-based Medicine for Long-term Multiple Sclerosis Treatment (PRISMS LTFU)
Douglas S Goodin

Function Room
14:00 – 17:00
ASEPA EEG EXAM PART 2
Examiners:
SH Lim
CT Tan
SY Kwan
T O'Brien

15:00 – 15:30 Coffee Break

15:30 – 16:30 **SYMPOSIUM ON NEUROMUSCULAR DISORDERS**

Chairpersons: *Yuk-wah Chan, Winnie Wong*

Pattern Recognition Approach to Muscle and Neuromuscular Junction Disorders
Richard J Barohn

How to Get the Best Out of Your Pathology Laboratory in Neuromuscular Diseases?
Ho-keung Ng

Treatment and Clinical Research in Myasthenia Gravis: How Far Have We Come?
Richard J Barohn

Neurodegeneration: the Processes

Raymond CC Chang[1,2,3], Jianfei Chao[1,4], Yuen-shan Ho[1], Mingfu Wang[4]
[1] Laboratory of Neurodegenerative Diseases, Department of Anatomy
[2] Research Centre of Heart, Brain, Hormone and Healthy Aging, LKS Faculty of Medicine
[3] State Key Laboratory of Brain and Cognitive Sciences
[4] School of Biological Science, Faculty of Science
The University of Hong Kong, Pokfulam, Hong Kong

While neuronal apoptosis has long been considered to be the major mode of neurodegeneration in chronic neurological disorders in Parkinson's disease, increasing lines of findings have demonstrated that neurodegeneration are mingle of autophagy, synaptic retraction, and axonal transport. Different survival and pro-apoptotic signalling pathways become biological targets for intervention. Apart from investigating the degenerative signalling in neurons, the responses of glial cells are important to determine the fate of dopaminergic neurons. Therefore, pharmacological interventions of neurodegenerative processes in Parkinson's disease can be on both glial cells and neurons. I will at first briefly introduce different modes of neurodegenerative processes.

As dopaminergic neurons are vulnerable to oxidative stress, prevention of neuronal loss in Parkinson's disease is mainly relied on anti-oxidant. However, any potential drug candidate which has simply anti-oxidative effect only may not be sufficient to be neuroprotective agent for Parkinson's disease. We have investigated and examined different small molecules from dietary supplement and food extracts. One of the targets we have initiated is the derivative of stilbene, oxyresveratrol. Parkinsonism mimetic is often the starting point of finding the neuroprotective agent against neurodegeneration in Parkinson's disease. We have investigated protective effects of oxyresveratrol against 6-hydroxydopamine (6-OHDA) neurotoxicity. Our results demonstrate that oxyresveratrol can penetrate into the dopaminergic neurons to antagonise free-radical production. It can also increase SIRT1 and survival signalling pathway, suggesting that neuroprotective effects of stilbene is not just anti-oxidation. The results lead us from the starting point to further investigate whether this kind of stilbene derivative can be developed into therapeutic agents against neurodegeneration of Parkinson's disease. As dietary supplement is generally accepted by the public, this may be a potential approach to prevent Parkinson's disease in the community.

Acknowledgement
The work on Parkinson's disease is supported by HKU Strategic Research Theme on Drug Discovery.

Genetics in Parkinson's Disease: Any Emerging Picture?

S 2

Yoshikuni Mizuno
Juntendo University School of Medicine, Tokyo, Japan

Up to 14 chromosome loci have been identified for different forms of familial Parkinson's disease (PD)—7 autosomal dominant (AD), 6 autosomal recessive (AR), 1 X-linked. The disease genes have been identified in 10 of them; *alpha-synuclein* for PARK1, *parkin* for PARK2, *UCH-L1* for PARK5, *PINK1* for PARK6, *DJ-1* for PARK7, *LRRK2* for PARK8, *ATP13A2* for PARK9, *Omi/HtrA2* for PARK 13, *PLA2G6* for PARK14, and *FBOXO7* for PARK15. For the remaining forms, candidate genes have been proposed, but still there are controversies which one is the real disease gene.

Alpha-synuclein plays a very important role not only in PARK1-linked PD but also in sporadic PD. Both missense mutations and multiplications of *alpha-synuclein* are known. Mutant alpha-synuclein proteins have increased tendency for self-aggregation and during the process of aggregation, still soluble oligomers of alpha-synuclein proteins are formed. Such species are believed to be toxic to intracellular organella such as synaptosomes, 26S proteasome and mitochondria. Increased amount of alpha-synuclein is suffice to cause nigral neurodegeneration; however, not all the patients with duplication of this gene will develop PD. Other genetic factors appear to play a role in the nigra neurodegeneration. Triplication of alpha-synuclein is almost always associated with Parkinsonism and dementia and diffuse Lewy body type of pathology.

Parkin is the disease gene for PARK2-linked early onset autosomal recessive PD. Our group found that parkin protein has an E3 ligase activity of the ubiquitin system. However, no explicit evidence for the accumulation of candidate parkin-substrates has been reported. Therefore, the exact molecular mechanism of nigral neuronal death in PARK2-linked PD is still to be investigated. In the respect, recent studies indicated interaction of parkin with PINK1, the disease gene for PARK6-linked PD. We recently have shown that 'RING1-inbetween RINGs' part of the parkin protein bound to PINK1 protein inhibiting the self-ubiquitination and destruction of PINK1 protein. PINK is essential for the integrity of mitochondria; thus parkin and PINK appear to work together to protect mitochondria from damage.

PARK8 is the most common familial PD transmitted as autosomal dominant. The disease gene was identified as *LRRK2*, which is a huge gene encoding a protein consisting of more than 2500 amino acids. The carboxyl half is the functional domain consisting of leucine rich repeat, ROC region, COR, MAPKKK and WD domains. The function of LRRK has not been well elucidated yet; ROCO region can bind GTP leading to the activation of serine-threonine kinase activity of this protein. And phosphorylation of some proteins by LRRK2 can be toxic to neurons and may down-regulate the neurite out growth. In fact, G2019S mutant and I2020T mutant LRRK2 proteins have increased kinase activity.

More newly discovered PARK proteins have unique functions; for instance, ATP13A2 is expressed in lysosomal membranes and has an ATPase activity; Omi/HtrA2 protein is another mitochondrial protein with a proteinase activity, PLA2G6 is a calcium-independent phospholipase releasing arachidonate from the membrane, and finally FBOXO7 protein is related to apoptotic pathways.

Finally there must be a common molecular mechanism for neurodegeneration in sporadic PD and familial PD. Further studies on familial PD may disclose pathogenesis of sporadic PD at a molecular level.

Therapeutic Implications of Modulations of Glutamatergic Neurotransmission in Models of Parkinson's Disease

S 3

Ken KL Yung
Department of Biology, Hong Kong Baptist University, Hong Kong

A specific and progressive loss of dopaminergic neurons in the substantia nigra pars compacta is the key pathology of Parkinson's disease. Glutamate excitotoxicity is suggested to involve in neuronal cell death of dopaminergic neurons and intervention of the glutamatergic neurotransmission is one possible means of therapy. My laboratory is focused on the pathological changes after the onset of Parkinson's disease and also on the development of novel treatments. We have employed animal model namely 6-hydroxydopamine-lesioned rat and neuronal cell models. Several recent advancements have been made. First, we have tested an approach of gene knockdown of glutamate receptors, namely the N-methyl-D-aspartate receptor (NR) subunits, in treatment of Parkinson's disease. After applications of NR specific small interfering (si)RNAs, motor symptoms of Parkinson's disease have been reduced. The siRNAs have been found to deliver a limited degree of neuroprotection to dopaminergic neurons. Second, we have also applied a neuroprotective antibiotic, namely ceftriaxone, to the models. Ceftriaxone, a beta-lactam antibiotic that can readily pass through the blood-brain barrier, has been shown to increase the expression of glial glutamate transporter GLT-1. After applications of ceftriaxone, motor symptoms in animals have been found to be reduced. Reduction in cell death of dopaminergic neurons has also been found. Therapeutic effects of ceftriaxone are brought by enhancement of GLT-1 expression which in turn reduces the excitotoxic levels of glutamate. Moreover, the above two therapeutic approaches can be combined to modulate glutamate homeostasis and form the basis for glutamate therapeutics. In summary, we anticipate developing new neuroprotective strategies of dopaminergic neurons that aim at multiple targets and may provide crucial advancements in pharmacological intervention of Parkinson's disease.

Acknowledgements
The present work was supported by HKBU262107, Hong Kong Research Grants Council, FRG06-07-II-26 and Mini-AoE project, Hong Kong Baptist University.

Neuronal Mitochondrial Uncoupling Proteins: Implications in Parkinson's Disease

S 4

Philip Ho
University Department of Medicine, The University of Hong Kong, Hong Kong

Parkinson's disease (PD) is a common disorder characterised by selective degeneration of dopaminergic neurons. Why and how it develops is unknown. Its current treatment does not address the underlying neuronal death, or reduce its progressive disability. A treatment strategy to modify its course involves reducing the harmful effects of mitochondrial dysfunction. Mitochondria are the main source of cellular energy (ATP). ATP production is coupled to oxidative phosphorylation, driven by the mitochondrial membrane potential (MMP) and produces harmful reactive oxygen species (ROS) as by-products. Uncoupling proteins (UCPs) belong to a family of mitochondrial solute carriers in the inner mitochondrial membrane, which partially dissipate this proton gradient in form of heat before it can be used to provide the energy for oxidative phosphorylation. Five homologues of UCPs have been identified (UCP1 to UCP5) and they are differentially expressed in various tissues. UCP1 is localised mainly in brown adipose tissue; UCP2 is ubiquitously expressed, at varying levels in different tissues including neurons; UCP3 is mainly found in skeletal and heart muscles; UCP4 and 5 are predominantly expressed in brain. Their physiological functions remain unclear. However, the 'mild uncoupling hypothesis' has been proposed to explain the protective functions of UCPs in alleviating oxidative stress through their uncoupling activities by dissipating the proton gradient and reducing ROS levels generated during oxidative phosphorylation. We focus to identify the linkages between mitochondrial dysfunction, and neuronal UCPs expression in parkinsonian models, by elucidating how they interact to overcome the harmful processes which lead to PD. Recently, we observed a differential modulation of UCP2, 4 and 5 expressions in MPP^+-induced toxicity in a human neuronal cell line, which we hypothesised as a potential protective cellular response to counteract the toxic insults. We have also demonstrated significant protection against MPP^+ and dopamine-induced cell death after stable overexpression of UCP4 and UCP5, by reducing oxidative stress and preventing ATP deficiency. The neuroprotective effects of UCP4 overexpression seem functionally linked with UCP2 expression. We have also identified major transcriptional elements which regulate UCP4 gene expression. Our findings may yield vital clues of how neuronal UCPs affect mitochondrial functioning. Modulation of neuronal UCP expression may lead to neuroprotective strategies to reduce the effects of mitochondrial dysfunction in not only PD, but also other neurodegenerative disorders, eg Alzheimer's disease, and ageing.

Glial Pathologies in Parkinsonism

S 5

Glenda Halliday
Prince of Wales Medical Research Institute and the University of New South Wales, Sydney, Australia

Glia outnumber neurons in the central nervous system (CNS) 10 to 1 and make up around 50% of brain volume. There are three main types of glia in the CNS (astrocytes, oligodendroglia and microglia) that provide neuronal support and homeostasis, form myelin, and actively participate in signal transduction. Glial pathologies always accompany neuronal degeneration. There are three major forms of neurodegenerative parkinsonism; Parkinson's disease (PD), multiple system atrophy (MSA), and progressive supranuclear palsy (PSP). Parkinson's disease is the most prevalent movement disorder, and MSA and PSP are approximately 5 times less prevalent than PD. Pathologically PD is characterised by neuronal α-synuclein deposition in Lewy bodies, MSA by α-synuclein deposition in oligodendroglia cytoplasmic inclusions (GCI), and PSP and corticobasal degeneration (CBD) by tau deposition in neurons and glia. Significantly different astrocytic reaction occurs in the different parkinsonian disorders. In PD there is minimal reactivity, although a significant proportion of the protoplasmic astrocytes accumulate α-synuclein in their cytoplasm. In MSA there is severe reactivity of fibrous astroctyes that is directly related to the severity of α-synuclein GCI formation. In PSP and CBD there is a severe reaction of the protoplasmic astrocytes that express parkin. The severity of this change correlates with neuronal tau deposition in PSP but not in CBD. Oligodendroglia pathology is diagnostic for MSA. Recent studies have shown that the oligodendroglial protein p25α relocates from the myelin to expanding oligodendroglial cell bodies prior to the development of GCI. This is associated with the expression of LRRK2 which degrades myelin basic protein (MBP) and demyelinates smaller caliber axons in the corticospinal and pontocerebellar pathways. Receptor-mediated activation of microglia occurs in response to any normal or abnormal change in the brain environment. Activated microglia will go on to become phagoctyic in response to significant perturbations such as infections and neurodegeneration. Phagocytic microglia concentrate in regions of cell loss in parkinsonian disorders, whereas reactive non-phagocytic microglia express parkin in response to the pathological protein deposition in these disorders. In MSA, the severity of reactive non-phagocytic microglia also correlates with the severity of fibrous astrogliosis and tissue loss. Overall, different glial changes occur in parkinsonian disorders supporting different underlying pathogenic mechanisms.

Managing Different Stages in Parkinson's Disease: an Update

S 6

Yoshikuni Mizuno
Juntendo University School of Medicine, Tokyo, Japan

Treatment of Parkinson's disease (PD) should be modified according to the manifestations and severities of the patients. Usually the initial 5-year period from initiation of the drug treatment, patients experience smooth improvement of Parkinsonian symptoms through the day. They do not experience wearing off, dyskinesia, or freezing phenomenon. In this early stage of the disease, close to 50% of dopaminergic terminals in the striatum is expected to be remaining and functioning. In this way, levodopa administered is taken up into the remaining dopaminergic neurons and converted to dopamine and stored into the dopaminergic vesicles. Then dopamine is released for striatal neurons when dopamine is really necessary and released dopamine is taken up back into the dopaminergic neurons. Thus these patients do not show wearing off or dyskinesia. Whereas in advanced PD patients, most of the nigrostriatal dopaminergine terminals are degenerated, particularly in the posterior putamen, which is important in the execution of motor functions. In such patients, most of levodopa given is unable to be taken up into dopaminergic neurons; they have to go to serotonergic terminals coming from the raphe nucleus or to the glia cells in the striatum. The serotonergic neurons have dopa-decarbosylase and serotonin storage vesicle. Levodopa can be synthesised to dopamine and dopamine is able to enter serotonin storage vesicles. But the release of dopamine from such serotonergic neurons may not be exactly the same in terms of motor execution. In addition, serotonergic neurons do not have dopamine transporters to re-uptake dopamine once released into the synaptic clefts. Regarding glia cells, they have dopa decarboxylase. Levodopa is taken up to neurons through glia cells. Therefore, there is a good reason to believe that fair amount of levodopa may stay in the glia cells because of degeneration of the dopaminergic neurons and certain amount of levodopa will be converted to dopamine within glia cells. However, glia cells do not have dopamine storage vesicles nor dopamine transporters for re-uptake. Thus once dopamine is synthesised within glia cells, synthesised dopamine may be rapidly released into the synaptic clefts and will not be re-uptaken to glial cells. Thus both serotonergic terminals and glia cells do not have a device to store dopamine once released into the synaptic clefts. Synaptic dopamine has to be metabolised by catechol-O-methyl transferase. This is what is going on in the striatum of advanced stage PD patients. Thus it seems to be inevitable to escape the development of wearing off in most of PD patients. The strategy of how to treat PD patients should be constructed by keeping on what is going on in the brain of a given patient.

Regarding the treatment of early stage PD, there has been debate on whether or not drug treatment of PD should be started early in the course of the disease or watch and wait until the disability reaches a certain level; because if levodopa is instituted too early, it may induce dyskinesia from early stage of the disease. However, recent trend seems to be in favour of early institution of the drug treatment. The brain has plasticity; if abnormal neuronal circuits from dopamine deficiency are restored toward normal from the early stage of the disease, brain has an ability to keep such improved condition that will result in long-term better condition of symptoms. Therefore, most of the PD specialists tend to start drug treatment in fairly early stage, if a given patient complains of certain difficulty in the activities of daily life. When the patient does not have cognitive impairment, available evidence suggests starting treatment with one of the non-ergot dopamine agonists. If the disability is very mild and both physician and patient are reluctant to start with a dopamine agonist, one can use a monoamine oxidase B inhibitor, which has only few side-effects and has modest symptomatic effect. When the patient already has cognitive impairment and/or hallucination/delusion, the evidence indicates to start the treatment with levodopa.

Management of numbers of motor as well as non-motor problems arising in the course of drug treatment of PD will be discussed in my talk.

Non-dopaminergic Degeneration in Motor Circuits and Their Impact on the Treatment of Parkinson's Disease

Glenda Halliday
Prince of Wales Medical Research Institute and the University of New South Wales, Sydney, Australia

The classic clinical triad of the motor features in Parkinson's disease (PD) are bradykinesia, rigidity and rest tremor, and the diagnostic pathology accompanying these features are a substantial loss of the dopaminergic pigmented neurons in the substantia nigra, and Lewy body inclusions in remaining brainstem pigmented neurons. Dopamine replacement therapies initially successfully treat these symptoms in many patients. Dopamine release within the putamen improves rigidity and bradykinesia, but not resting tremor in PD. This supports the dogma that different brain circuits mediate these different motor features. Volitional movements are achieved by descending neural drive from so-called 'motor cortical' centres that are not affected by PD. Two subcortical systems are crucial for adequate volitional movement: cortical interactions with the motor thalamus and the integration of information through the basal ganglia. The progression of rigidity and dopaminergic cell loss in the substantia nigra and dopamine terminal depletion in the putamen are extremely similar, with the severity of α-synuclein deposition in the degenerating substantia nigra inversely correlating with the amount of remaining dopamine terminals in the putamen. These correlations suggest a direct link between these parameters. While degeneration of the dopaminergic nigrostriatal pathway is used to diagnose PD, it is only one of three main regions in the motor system that degenerates to a similar degree in PD, and degeneration in these other regions is likely to contribute to other PD motor symptoms. The other two regions are glutamatergic and influence either the same basal ganglia region (caudal intralaminar thalamus projection to the putamen and caudate nucleus) as the nigrostriatal pathway or the same premotor cortical regions (presupplementary motor cortex projection to the supplementary and premotor cortices) as influenced by the basal ganglia output to thalamocortical relays. While bradykinesia is also responsive to dopamine replacement therapies, it has a different progression to that observed for rigidity and the loss of the nigrostriatal dopaminergic projection. The different dynamics may indicate the involvement of the presupplementary motor cortex degeneration in the generation of this clinical feature, consistent with its initial response to dopamine replacement therapy prior to the impact of degeneration in the presupplementary cortical region. From direct recordings, the resting tremor of PD appears to arise from spontaneous oscillatory activity in the ventrolateral anterior thalamus and lesions or high frequency stimulation of this region permanently improve PD resting tremor. In addition to the generation of the classic clinical motor triad by the degenerative changes in the motor system found in patients with PD, additional motor complications occur over time in association with levodopa replacement therapies. The exact mechanisms for these motor fluctuations remain unclear, but ongoing dopaminergic and non-dopaminergic degeneration in the critical motor system regions outlined, in concert with the neuronal remodelling that occurs in the putamen and caudate nucleus in response to the massive denervation of these structures, are likely to play a significant role. In this way both dopamine and non-dopamine lesions contribute to the cardinal motor features of PD.

Central Post-stroke Pain

S 8

Jong-sung Kim
Department of Neurology, Asan Medical Center, Seoul, Korea

Pain is one of the most troublesome sequelae of stroke, occurring in 19 to 74% of patients. A portion of this post-stroke pain is caused by the brain lesion itself; this is called 'central post-stroke pain (CPSP)'. Although the prevalence of CPSP among stroke patients is low (1-8%), the persistent, often treatment refractory painful sensations can be a major problem, decreasing the affected patient's quality of life. As the ageing population continues to increase, CPSP will become an even more important problem in the future. Although the pathogenesis of CPSP is not yet known, it has been suggested that underlying causes may include hyper-excitation in the damaged sensory pathways, damage to the central inhibitory pathways, or a combination of the two. Adrenergic antidepressants are currently the first-line drugs for CPSP, but their effect is frequently incomplete. Antiepileptics, such as lamotrigine, can be used as an adjunctive therapy, while GABAergic drugs, such as gabapentin or pregabalin, have recently emerged as a potentially useful therapy. Non-pharmacological treatments such as motor cortex stimulation or deep brain stimulation also appear to be useful in a certain group of patients. Additional studies are urgently needed to improve our understanding of the pathophysiology of CPSP and support the development of better treatment modalities.

Optimising Delivery and Outcome in Stroke Thrombolysis—Experience from Singapore

S 9

Bernard Chan
Department of Neurology, National University Hospital in Singapore, Singapore

Although intravenous (IV) tissue plasminogen activator (TPA) administered within 3 hours of stroke onset was proven an effective treatment for ischaemic stroke in the NINDS study published in 1995, only a minority of stroke patients received thrombolysis mainly due to late presentation. In Asian countries, delivery of thrombolysis is further impeded by shortage of neurologists, perceived risk of haemorrhage, and uncertainty of the optimal dosage to be administered. The National University Hospital in Singapore had a protocol to deliver IV TPA therapy for acute stroke since 1998, with restrictions in the upper age limit to 65 years and the maximum dose to 50 mg. Only 1 to 2% of ischaemic stroke patients were thrombolysed with mediocre outcomes. Since late 2006, the protocol was revamped with participation in the TPA roster restricted to stroke neurologists, more efficient triage of stroke patients, extension of upper age limit of treated patients, and use of standard TPA dose (0.9 mg/kg, maximum 90 mg). In addition, computed tomographic angiography and bedside transcranial Doppler have been increasingly used to locate the site of arterial occlusion and monitor response to treatment. These measures have enabled us to treat >10% of the ischaemic stroke patients presented to our hospital with IV TPA and achieve better outcomes (3-month mRS 1-2 in 59% vs 35%), despite the increased age (mean, 62 vs 55 years), more severe stroke (median NIHSS score, 15 vs 12) and higher TPA dose given (mean, 72 vs 46 mg) for our current patients, compared to patients treated earlier. Multivariate analysis revealed the use of standard TPA dose, rather than lower doses, is associated with functional independence at 3 months.

Acute Stroke Care in Singapore

S 10

Bernard Chan
Department of Neurology, National University Hospital in Singapore, Singapore

About 9000 acute stroke patients are hospitalised each year in Singapore, the majority in the five government restructured hospitals, of which three are teaching hospitals with in-house neurology and neurosurgery teams. Patients can choose among different ward classes to be admitted, which differ in the level of government subsidy. Ischaemic strokes are managed under neurologists, and haemorrhagic strokes under neurosurgeons. All hospitalised stroke patients are managed under stroke care paths, and stroke units have been established in some hospitals. Intravenous thrombolysis is provided at the three teaching hospitals, and in-house interventional neuroradiologists are available in two. Likewise, neurological high-dependency units and neurocritical care units have only been set up in the teaching hospitals. Comprehensive investigations including CT or MR neuroimaging; and vascular imaging by ultrasound, CT or MR modalities are performed in most stroke patients. As there has been a long-standing shortage of beds in acute hospitals, rehabilitation and discharge planning are initiated as soon as possible after hospitalisation. Most of the disabled stroke patients are transferred to community hospitals for a period of rehabilitation usually up to 1 month, but a few patients who require aggressive therapies undergo rehabilitation at the sole in-patient rehabilitation unit in Singapore. The Ministry of Health publishes a clinical practice guideline in stroke management, and regularly updates the average bill sizes of major diseases including stroke from different hospitals in its website. Audits on outcome and process indicators in hospital stroke management have been carried out periodically at the cluster or national level.

A Retrospective Review of Endovascular Treatment of Cerebral Aneurysm in Hong Kong

S 11

John CK Kwok[1], KM Cheng[2], WM Lui[3], KY Pang[4], CB Tan[5], Simon Yu[6]
[1] Kwong Wah Hospital, Hong Kong
[2] Queen Elizabeth Hospital, Hong Kong
[3] Queen Mary Hospital, Hong Kong
[4] Pamela Youde Nethersole Eastern Hospital, Hong Kong
[5] Tuen Mun Hospital, Hong Kong
[6] Prince of Wales Hospital, Hong Kong

Endovascular treatment for ruptured cerebral aneurysm was started as early as two decades ago in Hong Kong. It gained in popularity and volume of cases at the turn of the new millennium when new catheter and coils were made available in South East Asia. Following the publication of the International Subarachnoid Aneurysm Trial (ISAT) which demonstrated superior 1-year clinical outcomes associated with coiling in 2002, more aneurysms were treated among the six Hospital Authority endovascular units since then. However, many proponents of clipping have criticised these results for the lack of longer-term follow-up, particularly as related to the durability of coiling for preventing rebleeding, and because of the need for and risks of surveillance angiography and possible retreatment. These latter concerns, combined with the expense of detachable coils, have also raised questions about the cost-effectiveness of coiling, compared to clipping. In 2009, the Stroke Society of Hong Kong has invited the endovascular centres to present their past years' result of coiling in quarterly scientific meeting. These data will be grouped and to be presented in this annual meeting with highlights of the volume treated, site, rebleeding rate, and projection of future development of endovascular treatment of cerebral aneurysm in Hong Kong.

Current Neurovascular Practice in Sydney, 2009

Bernard Kwok
Prince of Wales Private Hospital, Sydney, Australia

The introduction of interventional neuroradiology into mainstream medical practice brought about a radical change in the delivery of neurovascular service in NSW. Following the publication of the International Subarachnoid Aneurysm Trial (ISAT) in 2002, the neurosurgical unit in Prince of Wales Hospital in Sydney, in cooperation with three other neurosurgical units within the SESIAHS, set up a multidisciplinary neurovascular unit (MDNVU) to manage patients with neurovascular disease. The composition of the MDNVU includes neurosurgeons (NS), interventional neuroradiologists (INR), and radiation oncologists (RO).

Surgical clipping of cerebral aneurysms started in 1927 making major advances in line with improvement of neuroanaesthesia, introduction of surgical microscope and clips, and improved surgical approaches. It has reached a plateau in its development in the late 80s and early 90s. On the other hand, interventional treatment of aneurysms started in the 70s and development in earnest in the 80s and early 90s with the Guglielmi detachable coil (GDC). Every ruptured cerebral aneurysm patient presenting to the four NS units as well as the draining hospitals within SESIAHS are discussed between the INR and NS to decide whether it is best to coil or to clip the aneurysm.

The MDNVU also meets on a weekly basis using teleconferencing to discuss cold cases, including unruptured aneurysms, arteriovenous malformations (AVM), cavernous angiomas (CA), and dural arteriovenous malformations (DAVM).

Whereas MDNVU is fairly recent, Stroke unit has been established much longer in Sydney. It is now a standalone unit separate from neurology or rehabilitation units in all major teaching hospitals and larger suburban as well as regional hospitals. Its composition and management algorithm will be discussed.

Status Epilepticus in 2009: What We Know and What We Don't

David Treiman
Barrow Neurological Institute, Phoenix, Arizona, US

What we know

Over 100 years ago Clark and Prout described dynamic changes in generalised convulsive status epilepticus (GCSE) that, in current neurological thinking, have only recently been recognised again. We now know that in untreated or inadequately treated GCSE, there is (1) a progressive decrease in convulsive activity, (2) a predictable sequence of electroencephalography (EEG) changes, (3) increasing refractoriness to treatment, (4) progressive neuronal damage, and (5) progressive severity of post-SE behavioural deficits. We have begun to recognise some, but not all, of the neurochemical changes that underlie these electro-clinical changes. These dynamic changes can be understood in the context of a physiologic definition of SE: a situation where any seizure-induced acute impairment of neurological function or alteration of brain physiology or chemistry does not recover to the pre-seizure state before another seizure occurs. Thus, in SE, by definition, the effects of repeated seizures are cumulative, which partially explains the dynamic progression of GCSE from overt convulsions, to subtle GCSE, to 'electrical' GCSE. In parallel, a predictable sequence of EEG changes from discrete electrographic seizures through continuous seizure activity, to periodic epileptiform discharges on a flat background occurs. These EEG patterns can be viewed a marker of the severity of the episode of GCSE at any given time.

Evidence is clear from both animal and human studies that progressive refractoriness of GCSE to pharmacological treatment is a result of attenuation of GABA-mediated inhibition, along with an exacerbation of glutamate-mediated excitation. Some of these effects are the results of post-synaptic receptor trafficking, with internalisation of GABA receptors and externalisation of NMDA receptors, but treatment refractoriness may also be due, in part, to a depletion of pre-synaptic GABA.

Non-linear dynamical analysis of the EEG suggests preceding a single seizure there is a transition from the normal chaotic state of brain electrical activity to a less chaotic state, in which there is a high degree of entrainment between EEG electrode pairs. In contrast to a single seizure, where the brain resets to a chaotic state once the seizure occurs, during SE entrainment persists, even after discrete seizures, thus suggesting that the pathophysiology of SE is fundamentally different from that of a single seizure.

A number of recent epidemiological studies have established how common SE is, with an annual incidence of 10.3-61/10^5. Status epilepticus is most common in neonates (135-156/10^5) and the elderly (14.6-86/10^5). Worldwide there are about 3 million cases of SE annually.

Current evidence is that lorazepam is the best drug for the initial treatment of GCSE. An effective SE treatment protocol is provided below. Several recent reports have suggested a role for VPA in the initial treatment of GCSE, but a direct comparison with lorazepam has not yet been done. Despite initial enthusiasm, levetiracetam does not appear to have role in the initial treatment of GCSE, most likely because of a delay in crossing the blood-brain barrier.

What we don't know

Although progress has been made in understanding SE, we still do not know what seizure termination mechanisms break down to allow seizures to rapidly recur during SE. We do not know the underlying mechanisms of the dynamic changes causing attenuation of convulsive movements, progression of EEG patterns in a predictable sequence, and progressive neuronal damage and behavioural deficits. We are only beginning to develop an understanding of what mechanisms to pursue to develop better anti-SE drugs and to prevent SE-mediated neuronal damage. We do not yet understand the mechanisms of EEG entrainment preceding seizures and why the EEG normally resets to a non-ordered chaotic state when a single seizure occurs, but fails to do so in SE. We are only beginning to understand how to use nonlinear dynamic analysis of the EEG to develop diagnostic tools with a high degree of sensitivity and specificity.

Treatment protocol for GCSE:

Time (min)	Treatment protocol
0	Establish the diagnosis by observing one additional seizure in a patient with recent seizures or impaired consciousness or by observing continuous behavioural and/or electrical seizure activity for >10 minutes.
	Start the EEG as soon as possible, but do not delay treatment unless EEG verification of the diagnosis is necessary.
5	Establish intravenous (IV) catheter with normal saline (dextrose solutions may precipitate phenytoin) — with fos-phenytoin either dextrose or saline is acceptable.
	Draw blood for serum chemistry, haematologic values, and AED concentrations. Check for hypoglycaemia by finger stick. If hypoglycaemia is present, administer 100 mg of thiamine (if indicated) followed by 50 mL of 50% glucose by direct push into the IV line.
10	Administer lorazepam (0.1 mg/kg) by IV push (<2 mg/min).
25	If status continues, start fos-phenytoin (20 mg/kg PE) by fast IV push (up to 150 mg PE/min) directly into the IV port nearest to patient; if only phenytoin is available, give by slow IV push (<50 mg/min); with either preparation monitor blood pressure and electrocardiogram during infusion.
	If status continues after 20 mg PE/kg fos-phenytoin (or 20 mg/kg phenytoin), administer an additional 5 mg/kg and, if necessary, another 5 mg/kg, to a maximum dose of 30 mg/kg.
60	If status persists, support respiration by endotracheal intubation; give phenobarbital (20 mg/kg) by IV push (<100 mg/min) or, preferably, start barbiturate coma: give pentobarbital (5-15 mg/kg) slowly as an initial IV dose to suppress all epileptiform activity and continue 0.5-5 mg/kg/h to maintain suppression; slow infusion rate periodically to determine cessation of seizure activity; monitor blood pressure, electrocardiogram and respiratory function. If unable to suppress all epileptiform activity, change to continuous infusions of propofol (1 mg/kg given over 5 min, then 2-4 mg/kg/h; adjust to 1-15 mg/kg/h) or midazolam (0.2 mg/kg bolus injection, followed by infusion of 0.05-0.5 mg/kg/h).
	Maintain full suppression of epileptiform activity (not a burst-suppression pattern) for 48-72 hours before beginning to the slow the infusion rate. Before beginning withdrawal of intravenous anaesthesia, adjust phenytoin serum concentration to 30 μg/mL; load phenobarbtial to achieve 100-150 μg/mL serum concentration. Maintain these levels as the anaesthetic agent is slowed. Levetiracetam is an alternative if PHT and/or PB are contraindicated. Load with 4 g IV, maintain with up to 1000 mg q 6 h IV.
	If epileptiform activity returns during lightening of the induced coma, increase the infusion rate of the anaesthetic agent (pentobarbital, propofol, or midazolam) to suppress all epileptiform activity for another 48-72 hours before attempting anaesthesia withdrawal again.
	Repeat as many times as necessary. Do not give up. Patients have recovered consciousness after >2 months of coma.

Pharmacogenomics of Epilepsy: an Update

S 14

Patrick Kwan
Prince of Wales Hospital, Hong Kong

In recent years, there has been an explosion of genetic research in epilepsy, including a search for genetic markers of response to antiepileptic drugs (AEDs) with the promise of improving drug safety and efficacy. Because of potential differences in genetic background, it is essential to carry out independent studies in individual ethnic groups. In line with this goal, a DNA bank of epilepsy patients has been established in Hong Kong since 2004 with participation from four major hospitals. To date clinical information and DNA samples have been collected from over 1200 patients and recruitment is ongoing.

Studies deriving from this consortium have already made important impact on our understanding of the pharmacogenomics of epilepsy in Chinese. In particular, confirmation of the locally common HLA allele, B*1502, as a strong predictor of carbamazepine-induced Stevens-Johnson syndrome contributed to the evidence base for the FDA's recommendation of HLA typing before prescribing the medication. Although a mechanism of HLA-B*1502 testing has been put in place in public hospitals in Hong Kong, the conventional genotyping platforms are relatively expensive and slow in result turnaround time. To facilitate clinical application, a more rapid and cost-effective HLA typing platform has been developed by local researchers, and a 'kit' for bedside use is under active development. Further territory-wide study will determine whether the HLA allele also predicts Stevens-Johnson syndrome induced by other AEDs.

Candidate gene association studies of the cohort have also led to the identification of genetic variants of drug transporters and neuronal sodium channels as potential markers of efficacy of AEDs, although replication studies are needed. An agnostic genome-wide approach is currently underway which is expected to shed lights on not only genetic markers of drug response but also of susceptibility to the development of epilepsy.

Neuropsychological Outcome Following Anterior Temporal Lobectomy for Epilepsy

S 15

Iris Chan
Department of Medicine, Queen Elizabeth Hospital, Hong Kong

Anterior temporal lobectomy (ATL) with resection of the mesial structures is known to be an effective intervention for patients with temporal lobe epilepsy. However, the majority of studies that have documented the neuropsychological consequences of this procedure have highlighted the potential risks of the procedure to neurocognitive abilities, and particularly to memory. Although the risks of ATL are widely recognised, some research found that only about one-third of patients experience a major postoperative neurocognitive deterioration. The majority of patients actually remain stable in terms of memory after the procedure, with some patients even indicating significant improvement. Anterior temporal lobectomy is currently performed in Hong Kong for the treatment of intractable temporal lobe epilepsy. A multidisciplinary team, which comprises neurologists, neuroradiologists, neuropsychologists and neurosurgeons, is responsible for the management of epilepsy surgery. A series of eight cases who received ATL at Queen Elizabeth Hospital is reviewed to examine their post-surgical neurocognitive functioning, in particular memory. Clinical implications of the findings will be discussed.

Reflex Seizures

S 16

Shang-yeong Kwan
Section of Epilepsy, Neurological Institute, Taipei Veterans General Hospital; Clinical Professor, National Defense Medical College, Taiwan; Assistant Professor of Neurology, National Yang-Ming Medical College, Taiwan

Reflex seizures are defined as epileptic seizures objectively and consistently demonstrated to be evoked by a specific afferent stimulus or by activity of the patient. Afferent stimuli can be: elementary, ie unstructured (light flashes, startle, a monotone) or elaborate, ie structured. Activity may be elementary, eg motor (a movement), or elaborate, eg cognitive function (reading, chess playing), or both (reading aloud). Reflex epilepsies refer to syndromes in which all epileptic seizures are precipitated by sensory stimuli, including idiopathic photosensitive occipital lobe epilepsy, other visual sensitive epilepsies, primary reading epilepsy and startle epilepsy. Various types of precipitating stimuli are found, including visual stimuli (flickering light, patterns, other visual stimuli), thinking, music, eating, praxis, somatosensory, proprioceptive, reading, hot water and startle.

In an analysis of the 63 patients with reflex seizures collected, there were 27 (43%) cases of praxis reflex epilepsy (26 Mahjong, 1 calculator), 12 (19 %) cases of somatosensory reflex epilepsy (6 tapping-startle, 2 tooth brushing, 2 shoeing, 2 hot water), 7 (11%) cases of photogenic epilepsy (3 television, 2 game, 1 computer, 1 strong light), 7 (11%) cases of auditory reflex epilepsy (6 with startle, 1 tone), and 5 (8%) cases of eating epilepsy. Complex stimuli (photogenic plus running) were noted in one patient. In classification of seizures, there were 24 (38%) cases of generalised tonic-clonic seizures, 6 (10%) cases of generalised tonic seizures, 2 (3%) cases of myoclonic seizures, 3 (5%) cases of atonic seizures, 2 (3%) cases of absence seizures (1 typical, 1 atypical), 11 (17%) cases of complex partial seizures (2 had simple partial seizures, 2 had secondary generalisation).

Demographic data and video-EEGs in some of these cases will be demonstrated. The latter includes eating-induced atypical absence seizure with atonic component, eating-induced complex partial seizure, somatosensory-induced generalised tonic seizure, complex stimui of photogenic plus running-induced atypical absence and auditory-startle–induced atonic seizure.

Women with Epilepsy: Preconception, Pregnancy and Post-delivery Care

S 17

Terence J O'Brien
Department of Medicine, The Royal Melbourne Hospital, The University of Melbourne, Parkville, Victoria, Australia

It has long been recognised that women with epilepsy who become pregnant while taking antiepileptic drugs (AEDs) have an increased risk of having a baby with a birth defect. However there has been much uncertainty about how much of this risk was a result of the AEDs, an effect of seizures, the genetic background, or other factors—including environmental. It was also uncertain about whether particular AEDs, doses or combinations are associated with a greater risk. Data from prospective pregnancy registers and well-designed hospital- and population-based epidemiological studies published over recent years are providing important data that has major relevance for clinical practice. Specifically sodium valproate and phenolbarbitone have been identified as being associated with a greater risk of birth defects compared to other AEDs, with the increased risk for the former particularly relating to higher doses (>1100 mg/day). Recent data also indicate that it is not polytherapy per se that is associated with a great risk than monotherapy, but rather when it is combined with valproate or barbiturates. There is also increasing concern amongst the epilepsy community about the potential for AED exposure to result in neurocognitive and neurobehavioural disabilities in children of women with epilepsy. The time window for effects on brain development is much longer than that for birth defects—extending throughout gestation, and even post-natally if the baby is breastfed. These often subtle deficits are more difficult to efficiently and objectively study than birth defects, but recent data are providing evidence that certain AEDs and doses may carry particular risks. It is also important to recognise that uncontrolled seizures also carry significant risks to the mother, unborn and born children, and these need to be balanced with the risk of the AEDs to the unborn child. Given that for many women there is no completely 'safe' option, clinicians need to engage the patient and their families, providing information regarding the latest scientific data, in order to facilitate them choosing the management plan that suits them best: preconception, during pregnancy and post-delivery.

Optimising Treatment Outcome for Multiple Sclerosis

S 18

Kwok-kwong Lau
Princess Margaret Hospital, Hong Kong

After suffering from the first demyelination, ie clinical isolated syndrome (CIS), not all patients will visit neurologists. Different multiple sclerosis (MS) patients will have different disease progression. The decision to give different therapies to different patients depends on the phase as well as the course of MS. From the study of natural history of CIS, 43% will progress to clinically definite multiple sclerosis (CDMS) in the first 5 years, 59% at 10 years, and 68% at 14 years.

In CHAMPS study, patients on interferon beta (IFNB) had half the chance of developing into CDMS when compared with those who were not on IFNB. The adjusted ratio rate=0.49 (95% CI, 0.33-0.73; P<0.001). The same pattern was noted in 5 years CHAMPS, with adjusted hazard ratio (HR)=0.57 (0.38-0.856). In ETOM study, the annual relapse rates were 0.33 and 0.43 in the active and placebo groups, respectively (P=0.045). In BENEFIT, the risk of CDMS was reduced in IFNB group by 50% (HR=0.50; 95% CI, 0.36-0.70). The risk for MS as defined by McDonald criteria was reduced by 46% (HR=0.54; 95% CI, 0.43-0.67). In PRECISE, patients who were on glatiramer acetate (GA) reduced the risk of CDMS by 45% compared with placebo (HR=0.55; 95% CI, 0.40-0.77).

The axonal damage in MS can occur early, with damage accumulates early in axonal processes. Immunohistochemistry which measures number of amyloid precursor protein (APP) has shown highest number of APP-positive axons in patients with less than 1-year duration. The disease modifying therapy (DMT) has the greatest advantage during highest degree of inflammation. The best time to give DMT is in the 'treatment window', or early phase of the disease.

There are two theories of approach, the 'escalation' and 'induction'. It is important to ascertain 'where' the patient may have been in the treatment window. If patient is in the early phase, 'escalation' treatment is more appropriate. In the later phase, the disease may be actively progressing and patient may not have enough time to exert their full effect. 'Induction' is more suitable for the later phase.

Evidence-based Medicine for Long-term Multiple Sclerosis Treatment (PRISMS LTFU)

S 19

Douglas S Goodin
Department of Neurology, University of California, San Francisco, United States

Establishing the long-term benefit of therapy in many chronic disease states like multiple sclerosis (MS) has been a challenge. Randomised, controlled studies typically judge therapeutic effectiveness on the basis of several short-term outcomes although the relationship between these outcomes and long-term function has not been established. There have been several long-term follow-up (LTF) studies of disease-modifying therapies (DMTs) including the interferon betas and glatiramer acetate. Each of these LTF studies has reported that long-term therapy with DMTs provides substantial long-term benefit. Nevertheless, each of the trials has also had a varying possibility of bias that often impact the non-randomised designs that are necessary for LTF studies. Nevertheless, several methods of bias reduction are available and these methods need to be incorporated into the design of LTF trials. To remove ascertainment bias, the baseline variables need to be compared between groups who participated in the LTF data and those that did not. Second, the bias of informed censoring needs to be taken into account. This bias is due to the fact that patients doing well on therapy will tend to stay on therapy whereas those who are not doing well will tend to drop out. A simple method to account for this bias is to measure exposure as a medication possession ratio (MPR) in which exposure is measured as the time a person actually was on medication divided by the time they could have been on therapy. Finally, as pointed out by Trajano and colleagues in Italy, propensity scoring can be used to reduce the bias of treatment selection. Once these methods have been employed, however, there is convincing evidence both that the short-term measures of clinical attacks, disability, and MRI lesions correlate significantly with long-term outcome that DMTs provide a dramatic benefit on long-term outcome.

Pattern Recognition Approach to Muscle and Neuromuscular Junction Disorders

Richard J Barohn
Department of Neurology, University of Kansas Medical Center, Kansas City, KS, US

The pattern recognition approach to disorders of muscle and of the neuromuscular junction is a simple clinical tool that allows the clinician to narrow the diagnostic possibilities down before any laboratory tests are done. The goals for the diagnostic process are to localise the lesion, to find the cause of the lesion, and to come up with a management plan. In order to accomplish these goals, the clinician asks six key questions in the course of the initial history and physical examination. The first question is, "Does the patient have 'negative' or 'positive' symptoms and signs?" Second, the clinician asks temporal questions about weakness, pain, and stiffness. Third, "What is the distribution of weakness? Stiffness?" Fourth, "Are there triggering events for episodic weakness, pain, stiffness?" Fifth, "Is there a family history of a myopathic disorder?" Finally, "Are there associated systemic symptoms or signs?"

After answering these questions, the clinician is ready to place the patient with a muscle or neuromuscular junction disorder into one of 10 possible patterns. The first pattern is proximal 'limb-girdle' weakness (acquired or hereditary). Pattern 2 is distal weakness and includes a variety of distal myopathies. The third pattern is proximal arm/distal leg weakness or the scapuloperoneal pattern. This pattern includes facioscapulohumeral dystrophy and scapuloperoneal myopathy and several other myopathies. Pattern 4, distal arm/proximal leg weakness, is the pattern for inclusion of body myositis, and predominantly involves knee extensors and forearm and finger flexors. This pattern is also occasionally seen with myotonic dystrophy. Pattern 5 is ptosis with or without ophthalmoplegia and can be subdivided into patients without diplopia (oculopharyngeal muscular dystrophy and mitochondrial myopathies) and those with diplopia (neuromuscular junction diseases). Pattern 6 is isolated neck extensor myopathy and a variety of other disorders of muscle and neuromuscular junction. Pattern 7 is bulbar weakness, including tongue and pharyngeal muscles and produces dysarthria and dysphagia. Pattern 8 is episodic pain, weakness, myoglobinuria with trigger. This can be related to exercise or not related to exercise. Pattern 8 is due to glycogen and fat metabolic defects and a variety of drugs. Pattern 9 is episodic weakness delayed or unrelated to exercise, and involves channelopathies such as the various forms of periodic paralysis. Pattern 10 is stiffness or decreased ability to relax, and also involves channelopathies producing myotonia and myotonic dystrophy.

It is at this point that further testing options are considered, such as blood tests (including genetic studies), electromyography, and muscle biopsy.

How to Get the Best Out of Your Pathology Laboratory in Neuromuscular Diseases?

S 21

Ho-keung Ng
The Chinese University of Hong Kong, Hong Kong

As neurology residencies in Hong Kong do not involve a period of neuropathology training, there is a need for neurology trainees to know something about basic histology and the functioning of a pathology laboratory, in addition to knowledge gleaned from textbooks about the specialised pathology of neuromuscular diseases. This is important not only because pathologic diagnoses of neuromuscular diseases are a combined clinical and laboratory effort, and each side needs to understand the other, but also there is a need for realistic expectations for specificity of diagnoses, turnaround time, preparation of tissues, realistic requests for special stains and an understanding of the use and limitations of electron microscopy. Some understanding of the cost-effectiveness of various special examinations, in this day and age of awareness of health economy, is also necessary. Pathology diagnoses of paediatric neuromuscular diseases are nowadays often superseded or complemented by genetic tests, whenever they are available. It will be ideal too if those carrying out the actual biopsies, eg neurosurgeons or orthopedic surgeons, have a basic knowledge too. The difference between the diagnostic implications for adult and paediatric neuromuscular diseases also needs to be understood. The following internet sites will be of help to clinicians: GeneClinics (http://www.geneclinics.org), GeneTests (http://www.genetests.org), Neuromuscular Disease Centre (http://www.neuro.wustl.edu/neuromuscular).

Treatment and Clinical Research in Myasthenia Gravis: How Far Have We Come?

S 22

Richard J Barohn
Department of Neurology, University of Kansas Medical Center, Kansas City, KS, United States

Myasthenia gravis (MG) can now be well managed with relatively safe and effective therapies. Prior to 1960 mortality for MG was approximately 30%. In the current era mortality should be less than 5%. Major therapeutic advances by decade were: physostigmine and thymectomy (1930s); mechanical ventilation (1950s); corticosteroids and plasmapheresis (1960s); azathioprine (1960s-1970s); cyclosporine (1980s); intravenous gamma globulins (1980s-1990s); and most recently mycophenolate mofetil (1990s-2000s). Modern management of MG involves a graded approach, beginning with cholinesterase inhibitors for mild symptoms and advancing to immunomodulating medications for more severe weakness. We now have several immunomodulating agents from which to choose: selection is based largely on time to clinical effect and adverse effects. The various treatment modalities that are available all have their limitations. In addition, some controversies remain regarding the effectiveness of some of the commonly used MG treatments. Recently completed and ongoing clinical trials suggest that there is still equipoise regarding the benefit of mycophenolate mofetil and thymectomy. A trial of intravenous immunoglobulin showed benefit compared to placebo. Chronic monthly plasmapheresis is occasionally useful in difficult-to-manage patients. Intravenous access is often made easier through the placement of arteriovenous fistulas. A multicentre, placebo-controlled, therapeutic trial of oral methotrexate in steroid-dependent patients is underway. A randomised international trial of thymectomy is also in progress. An industry-funded study is also in progress using an intravenous inhibitor of complement. The future appears to be promising, with clinical trials involving novel immunotherapeutic strategies.

FP 1

Expedited Stroke Triage Pathway is Key to Shorten Door-to-needle Time in Delivery of Thrombolysis Treatment

Alexander YL Lau, Thomas Leung, Yannie OY Soo, Eddie Wong, Anne YY Chan, Lisa Au, Vincent Ip, Cecilia Leung, Venus Hui, Wai-ching Shum, Lawrence KS Wong
Division of Neurology, Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong

Background: Thrombolysis for hyperacute stroke is a proven therapy and is an evolving standard of care in Hong Kong, though currently only a small percentage of stroke patients received such treatment. We explored means to improve stroke thrombolysis service and to identify access blocks to thrombolysis delivery by examining the stroke thrombolysis triage pathway and thrombolysis registry data.
Methods: We used prospective data from a stroke thrombolysis registry established in a tertiary hospital since October 2008. All thrombolysis calls for hyperacute stroke initiated by the Accident and Emergency Department were recorded. Data that included symptom-to-door, door-to-stroke-team, door-to-CT-interpretation, door-to-needle, and onset-to-thrombolysis times, and thrombolysis-related complications were analysed and compared against the time frames recommended by the National Institute of Neurological Disorders and Stroke (NINDS). Reasons for not giving thrombolysis were explored.
Results: From October 2008 to July 2009, we received 79 thrombolysis calls and gave intravenous tissue plasminogen activator (IV TPA) to 12 patients. The mean door-to-stroke-team and the door-to-needle times for IV TPA patients were 36 (range, 5-97) and 81 (42-131) minutes, respectively; both were 20 minutes longer than that recommended by NINDS. The average NIHSS for patients received IV TPA was 17 (6-30). The mean onset-to-treatment time was 137 (57-190) minutes. The most common reason for ineligibility of IV TPA was presentation beyond thrombolysis time window, which included wake-up strokes.
Conclusion: A dedicated stroke triage pathway and a neurologist-led thrombolysis team may ensure an efficient delivery of thrombolysis therapy. There is a need to improve door-to-stroke-team time in order to increase thrombolysis eligibility.

FP 2

The Application of Wavelet Technology in the Interpretation of Scalp Electroencephalogram

Howan Leung[1], Anne YY Chan[1], Alexander YL Lau[1], Ka-lau Leung[2], Cannon XL Zhu[3], Danny TM Chan[3], Patrick Kwan[1], Lawrence KS Wong[1]

[1] Division of Neurology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong

[2] Department of Surgery, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong

[3] Department of Neurosurgery, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong

Background: The wavelet theory is a mathematical tool with applications in signal processing. Wavelet transform refers to the process of decomposing and reorganising information based on the properties of a mother wavelet. The transformed signals may provide useful clinical applications such as the interpretation of scalp electroencephalogram (EEG) in clinical neurology. Wavelet transforms may be classified into discrete wavelet transform (DWT) and continuous wavelet transform (CWT). The use of these two different types of algorithms is tested and compared in this study.

Methods: Twelve patients with Engel Class I/IIa outcome following temporal lobe surgery (1 year) were selected with one to three ictal EEG records analysed per patient (n=25 seizures). With method A, the EEG signals were denoised with DWT algorithms using biorthogonal wavelet bior 3.9 and scale selection of 4. The resultant signals were fed into an algorithm which calculates normalised absolute slopes. With method B, the EEG signals were decomposed with CWT algorithms using biorthogonal wavelet bior 3.9 at scale 32. The normalised coefficients were computed for the transformed signals. Each seizure epoch was designated a localisation outcome (temporal, frontal, parietal, or occipital) and lateralisation outcome (left or right) based on each of the two methods (A and B). The threshold for each method is set as >2.5 of standard deviations from baseline EEG activities.

Results: Using method A, 21 (84%) of 25 seizures were correctly localised and 23 (92%) of 25 seizures were correctly lateralised. Using method B, 18 (72%) of 25 seizures were correctly localised and 21 (84%) of 25 seizures were correctly lateralised. The DWT algorithm specialises in denoising the EEG signals and requires the calculation of absolute slopes. The CWT algorithm specialises in decomposition of EEG signals and does not require the calculation of absolute slopes, although both methods require normalisation.

Conclusion: The application of wavelet technology in the interpretation of scalp EEG is feasible in clinical neurology. The DWT algorithm performs better than the CWT algorithm in terms of localisation and lateralisation of seizure activities in this pilot study.

FP 3

Double-blind Randomized Control Trial of Acupuncture for Autistic Spectrum Disorder

VCN Wong[1], WX Chen[1], WL Liu [2]
[1] Division of Child Neurology/Developmental Paediatrics/Neurohabilitation, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[2] Tung Wah Group of Hospitals, Clinical Centre for Teaching and Research in Chinese Medicine, The University of Hong Kong, Hong Kong

Objective: To study the efficacy, safety, and compliance of short-term electro-acupuncture (EA) for children with autism spectrum disorder (ASD).
Methods: This was a randomised, double-blind, sham-controlled, clinical trial. Children with ASD were randomly assigned to EA group (n=30) or sham electro-acupuncture (SEA) group (n=25) matched by age and severity of autism. The EA group received EA for selected acupoints while SEA group received sham EA to sham acupoints. A total of 12 acupuncture sessions over 4 weeks were given. Primary outcome measures included WeeFIM, Pediatric Evaluation of Disability Inventory (PEDI), Leiter International Performance Scale–Revised (Leiter-R), Clinical Global Impression–Improvement (CGI-I) scale. Secondary outcome measures consisted of Aberrant Behavior Checklist (ABC), Ritvo-Freeman Real Life Scale (RFRLS), Reynell Developmental Language Scale (RDLS), and standardised parental report. Data were analysed by Mann-Whitney test.
Results: There was significant improvement in language comprehension domain of WeeFIM (P=0.02), self-care caregiver assistant domain of PEDI (P=0.028), and CGI-I (P=0.003) in the EA than SEA group. As for parental report, the EA group also showed significantly better social initiation (P=0.01), receptive language (P=0.006), motor skill (P=0.034), coordination (P=0.07), and attention span (P=0.003). More than 70% children with ASD adapted acupuncture easily, while 8% had poor acupuncture compliance. Mild side-effect with minor superficial bleeding or irritability during acupuncture was found.
Conclusion: A short 4 weeks (12 sessions) course of EA is useful to improve the specific function in children with ASD, especially for language comprehension and self-care ability.

FP 4

Evaluation of Perfusion Computed Tomography in Patients with Multiple Large Artery Atherosclerosis

Yannie OY Soo[1], Thomas Leung[2], Henry Mak[1], Simon Yu[1], Wynnie Lam[2], Lawrence KS Wong[2]
[1] Prince of Wales Hospital, Hong Kong
[2] Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

Background: Perfusion computed tomography (PCT) is commonly used in hyperacute stroke for evaluation of penumbra in selection of patients for thrombolysis. Most data are from patients with cardioembolic stroke and single-vessel large artery atherosclerosis where a normal contralateral unaffected vascular territory is available for comparison of perfusion parameters. Scarce data regarding the use of PCT in patients with multiple large artery atherosclerosis are available. The aim of this prospective study was to evaluate the use of PCT in assessing perfusion deficit in patients with multiple large artery atherosclerosis in the late subacute phase of stroke.
Methods: A total of 49 consecutive patients admitted electively for digital subtractive angiography and stenting for symptomatic moderate-to-severe intra- or extra-cranial large artery atherosclerosis during February 2006 to March 2007 were recruited. Perfusion computed tomography was performed before and 1 month after procedure. Hypoperfusion was defined as area with prolonged mean transit time—cerebral blood volume mismatch by >20%.
Results: Atherosclerosis affected single vascular territory in 18 patients, and multiple vascular territories in 31 patients. Hypoperfusion was observed in 35 (71.4%) patients, up to 226 days post-stroke. Hypoperfusion occurred in territories with symptomatic stenosis in 33 (67.3%) patients. Among patients with stenosis affecting multiple vascular territories, hypoperfusion was observed in areas with asymptomatic stenosis in 9 (29.0%) patients. Forty-four patients underwent stenting. Post-stenting, 14 (43.8%) patients had complete resolution of hypoperfusion, nine (28.1%) patients had partial resolution.
Conclusion: Hypoperfusion is commonly observed in patients with symptomatic and asymptomatic severe large artery atherosclerosis weeks to months after stroke, and may be reversed with stenting. Caution should be taken when interpreting PCT in patients with severe stenosis affecting bilateral anterior circulation, where a normal contralateral counterpart is not available for comparison.

FP 5

Clinical Utility of National Institutes of Health Stroke Scale (NIHSS) in Screening Patients with Acute Stroke for Receiving Recombinant Tissue–Plasminogen Activator

May YN Mok, Sonny FK Hon, Richard Li, CN Lee, Eric SW Yeung, M AuYeung, CM Cheung, TH Tsoi
Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong

Background/Objective: To explore whether pre-treatment National Institutes of Health Stroke Scale (NIHSS) is important in screening suitable patients for receiving recombinant tissue–plasminogen activator (rt-PA) treatment in acute ischaemic stroke.
Methods: We conducted a retrospective review on the use of rt-PA treatment for 56 acute ischaemic stroke patients from our stroke database in a Hong Kong regional hospital from year 2003 to 2008. All patients received rt-PA had pre-treatment, 24 hours post-treatment and upon discharge NIHSS assessment performed and all data were collected prospectively and entered in the databank. The 30-day mortality rate and outcomes at 3 months were determined. Good outcome was defined as modified Rankin Scale score (mRs) <2. We sought to identify the relationship between pre-treatment NIHSS and the outcomes in acute stroke patients treated with rt-PA.
Results: The mortality rate at 30 days in patients with baseline NIHSS score >20 and >25 was 33.3% and 40%; the 3-month mortality rate was 37% and 46.7% respectively. The chance of good outcome at 3 months from stroke onset with baseline NIHSS score >20 and >25 was 33.3% and 26.7%, respectively. Among elderly patients of age >80, the 30-day mortality rate was 37.5% if NIHSS score >20; 33.5% if score >25. At 3 months, the chance of good outcome was 22.2% and 16.7% respectively. In the whole cohort of patients treated with rt-PA, the 30-day mortality rate was 16% and 51.8% had good outcomes.
Conclusion: NIHSS assessments performed before rt-PA treatment can be used to predict the 30-day mortality and long-term outcome among survivors. Irrespective of age, the NIHSS score of >25 and >20 are also strong predictors of death or poor functional outcome.

FP 6

Autonomic Dysfunction on Functional Outcome After Acute Ischaemic Stroke

L Xiong, Howan Leung, XY Chen, JH Han, Thomas Leung, Yannie OY Soo, Edward Wong, Anne YY Chan, Alexander YL Lau, Lawrence KS Wong
Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

Background/Objectives: Impaired autonomic function is common in the acute poststroke phase but little is known about its effects on functional outcome after acute ischaemic stroke. This study sought to investigate the impact of autonomic dysfunction by Ewing's classification on functional outcome 2 months after acute ischaemic stroke.
Methods: A total of 34 consecutive acute ischaemic stroke patients within 7 days after onset and 37 disease controls were enrolled. On admission, autonomic function was assessed by Ewing's battery tests. Stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS), autonomy in activities of daily living by the Barthel Index (BI), and global disability by the modified Rankin Scale (mRS). Barthel Index and mRS were also evaluated 2 months after ischaemic stroke onset.
Results: On admission, eight patients were diagnosed as minor autonomic dysfunction and 26 patients as relatively severe autonomic dysfunction. The prevalence of autonomic dysfunction in ischaemic stroke patients, which was 76.5%, was higher than that in controls which was just 21.6%. Ischaemic stroke patients showed impairment of parasympathetic function tests (all $P<0.05$) in comparison with controls. Two months after stroke onset, the mean BI score of patients with minor autonomic dysfunction and severe autonomic dysfunction increased from 76.3±15.3 on admission to 95.0±7.1, 66.5±15.2 on admission to 74.8±15.9 respectively. The mean BI score after 2-month stroke onset in patients with severe autonomic dysfunction was lower than that in patients with minor autonomic dysfunction ($P<0.05$).
Conclusion: Autonomic dysfunction occurs in acute stroke patients. Relatively severe autonomic dysfunction is related to an unfavourable functional outcome in patients with acute ischaemic stroke.

FP 7

Ketogenic Diet Programme for Children with Intractable Epilepsy in the Hong Kong West Cluster—13-Year Experience

Ada WY Yung, Virginia CN Wong
Division of Child Neurology/Developmental Paediatrics/Neurohabilitation, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital/Duchess of Kent Children's Hospital, The University of Hong Kong, Hong Kong

Background: The Ketogenic Diet (KD) is a high-fat, adequate-protein (1g/kg/day), low-carbohydrate diet that has been used for the treatment of intractable epilepsy since the 1920s. It is calorie restricted and traditionally is started in the hospital after 1 to 2 days fasting period. It does not cause sedative effects and provides an appealing alternative to other therapies, especially for patients with multiple antiepileptic drugs. Ketogenic Diet can be provided as the classical diet, which is more palatable, or with modification using gradually increasing percentages of medium-chain triglycerides, which may potentially induce more gastro-intestinal upset and diarrhoea. Glucose transporter 1 deficiency syndrome and pyruvate dehydrogenase deficiency are clear indications for the use of KD. Ketogenic Diet can be tried for epileptic syndromes such as infantile spasm, tuberous sclerosis complex, myoclonic-astatic epilepsy (MAE), severe myoclonic epilepsy of infancy (SMEI or Dravet syndrome), and Rett syndrome.
Methods: We reviewed the KD programme provided for children with intractable epilepsy in Hong Kong West Cluster (HKWC; Queen Mary Hospital/Duchess of Kent Children's Hospital). The Keto-team in HKWC is responsible for counselling and managing patients referred for trial of KD. Team members include child neurologist, epilepsy nurse, dietitian, clinical psychologist, and medical social worker. The self-initiated development of the HKWC KD programme had gradually evolved as two phases—Phase 1 (1996-2002) involving the use of medium chain triglyceride (MCT) diet; Phase 2 (2002-2009) with the use of classical KD for a more palatable diet and thereby improvement in compliance.
Results: Phase 1 (1996-2002) involved the trial of MCT diet for 10 patients (aged 8 months to 16 years). Duration of retention of the KD ranged from 1 month to 2 years. The reasons for discontinuation of KD included poor compliance, gastro-intestional upset, and intolerance of the diet with diarrhoea. Phase 2 (2002-2009) involved the use of classical KD. We actively recruited 24 children with intractable epilepsy for trial of KD programme. However, parents of 16 patients (aged 4 to 16 years) refused to participate into our KD programme. A common reason was the difficulty in preparing Chinese KD meals. Eight patients (aged 21 months to 7 years) were enrolled into our KD programme. Most were younger children aged <3 years (n=5) with naso-gastric tube feeding. Of these eight children, four (50%) had been maintained on the classical KD for ≥2 years, with >50% seizure reduction.
Conclusion: In the next phase of development (Phase 3), older children with intractable epilepsy will be recruited. Due to the difficulty in meal preparation, commercially available milk powder will be utilised.

FP 8

A Study of Cerebrospinal Fluid Neurotransmitters Assay in Children with Undiagnosed Neurological Diseases in Hong Kong

CW Fung[1], S Siu[2], G Poon[1], A Kwok[1], PT Cheung[1], L Low[1], C Mak[2], S Tam[2], VCN Wong[1]
[1] Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, Hong Kong
[2] Division of Clinical Biochemistry, Queen Mary Hospital, Hong Kong

Background: Paediatric neurotransmitter diseases (PNDs) are a group of disorders with a wide clinical spectrum of presentations including neonatal seizures, unexplained movement disorders such as dystonia, rigidity or ataxia, eye abnormalities including oculogyric crises, convergence spasm, ptosis or other intermittent ocular movement abnormalities, and autonomic symptoms like sweating, temperature instability, hypoglycaemia and hypothermia.
Methods: From 2004 to 2009, 114 children, aged 2 days to 33 years, with undiagnosed neurological diseases underwent lumbar puncture. Patients had one or more of the following symptoms: movement disorders, mental retardation/cognitive decline, epilepsy and spasticity which might be suggestive of disorders of biopterin, catecholamine and serotonin metabolism or cerebral folate deficiency. Extensive workup was unrevealing which included neuroimaging, cytogenetic studies, preliminary blood and urine for metabolic investigations. From 2004 to 2007, cerebrospinal fluid (CSF) was sent to the Division of Clinical Chemistry and Biochemistry, University Children's Hospital Zurich, Switzerland (Dr N Blau) for neurotransmitters assay. From 2007 onwards, the analysis was performed in the Division of Clinical Biochemistry, Queen Mary Hospital, Hong Kong.
Results: The presenting features of our cohort included various combination of clinical symptoms such as dystonia/rigidity, epilepsy which could be intractable, cognitive regression, global developmental delay/mental retardation, oculogyric crises, spasticity and hypotonia. Ten (8.8%) patients had abnormal neurotransmitters profile compatible with 6-pyruvoyl-tetrahydropterin synthase (PTPS) deficiency (n=5), tyrosine hydroxylase (TH) deficiency (n=2), idiopathic cerebral folate deficiency (CFD; n=2), aromatic L-amino decarboxylase deficiency (AADC) deficiency (n=1). Ultimate diagnosis was confirmed by genetic study in all patients with PTPS deficiency, TH deficiency and AADC deficiency. Two patients with CFD showed elevated autoantibodies against folate receptor (FR) confirming the diagnosis. Treatment was commenced in all 10 patients. One patient with PTPS deficiency revealed complete resolution of a parkinsonism state after replacement with tetrahydrobiopterin and L-dopa/carbidopa with normal intelligence. Another patient with PTPS deficiency only showed normalisation of hyperphenylalaninaemia without obvious clinical improvement with still significant generalised dystonia and moderate mental retardation. The remaining three patients with PTPS deficiency showed no neurological signs but with mild learning problem. One patient with TH deficiency demonstrated marked improvement in her dystonia and oculogyric crises after treatment with L-dopa/carbidopa and significant developmental progress. Another patient with TH deficiency did not reveal definite improvement and developed drug-induced dyskinesia. The child with CFD showed no more regression in cognitive and motor functions after replacement with folinic acid. His younger brother, who was nearly asymptomatic except mild spasticity over both lower limbs, did not have further deterioration in neurological functions after treatment. The patient with AADC deficiency was just started on bromocriptine and vitamin B6 treatment.
Conclusion: Paediatric neurotransmitter disease, a group of potentially treatable neurometabolic diseases, should be considered in any child with unexplained neurological symptoms including movement disorder, cognitive regression, oculogyric crises and spasticity. Early identification and treatment will improve morbidity and mortality.

D 1

Prediction of Spontaneous Haemorrhagic Transformation of Acute Major Cerebral Infarcts by Magnetic Resonance Imaging with Susceptibility-weighted Imaging Sequence

Hiu-fai Chan
Department of Medicine, Queen Elizabeth Hospital, Hong Kong

Background: Susceptibility-weighted imaging (SWI) technique has emerged as a sensitive neuroimaging modality in the detection of cerebral haemorrhage. We hypothesised that it may have a role in the prediction of spontaneous haemorrhagic transformation (HT) in patients with acute major ischaemic stroke.

Objectives: To assess if SWI can predict HT and neurological deterioration in Chinese patients with massive cerebral infarcts.

Methods: We prospectively examined 21 patients who were diagnosed with acute cerebral infarcts with a National Institutes of Health Stroke Scale (NIHSS) score of ≥8. Clinical assessments were performed at enrolment, on day 1, 7 and 90 after stroke onset. Computed tomographies (CTs) of the brain were performed before admission. The recruited patients then received SWIs and conventional magnetic resonance imagings (MRIs) of the brain within 48 hours after symptom onset. Follow-up computed tomographies (CTs) were performed 5 to 7 days after stroke onset to document the development of HT.

Results: Between 1 August 2008 and 28 February 2009, 21 patients were recruited. The overall frequency of HT detected on either follow-up CT or MRI was 66.67%. The SWI detected HT in 11 patients whereas CT detected HT in seven patients. Loss of lentiform nucleus shown on initial CT (78.57% vs 14.29%; P=0.02) and early parenchymal contrast enhancement shown on MRI (71.43% vs 14.29%; P=0.01) were found to be associated with HT formation. Subsequent development of symptomatic HT was less likely in patients with absence of HT shown on early SWI. No MRI parameters were reported to carry a predictive value in late HT. Parenchymal haemorrhage type 2 (PH-2) was the only HT type associated with symptomatic bleeding (100% vs 15.79%; P=0.048). Haemorrhagic transformation, especially PH-2, was linked to poor functional status and neurological deterioration but its relationship with 3-month mortality was not established.

Conclusion: In conclusion, SWI and MRI appeared to be a promising approach in the prediction of HT, especially symptomatic HT, after acute major ischaemic stroke. It might be useful to provide clues in the stratification of ischaemic stroke patients at risk of symptomatic HT. Future trials are warranted to evaluate the value of SWI and MRI in considering early initiation of anti-platelet therapy in patients with acute massive cerebral infarcts.

D 2

A Study on Anticoagulant Prescription after Acute Stroke in Non-valvular Atrial Fibrillation Patients in the Chinese Community

Cynthia Chen
Department of Medicine, Alice Ho Miu Ling Nethersole Hospital, Hong Kong

Background: Warfarin has been shown in research literature to be more effective than aspirin for prevention of thromboembolic events in patients with atrial fibrillation (AF). However, many studies in western countries suggest that anticoagulant therapy is under-utilised in patients with AF, and the reasons behind this are multifactorial. Several reasons against this treatment have been identified as severe disability, frailty, high risk of falls, and limited life expectancy. However, study data in Chinese communities are lacking.
Objective: To identify the reasons ethnic Chinese stroke patients with non-valvular AF in Hong Kong not treated with anticoagulant therapy, and try to identify issues that can be addressed to improve treatment rate.
Methods: A retrospective study was carried out to include acute stroke patients with non-valvular AF who were admitted to the Acute Stroke Unit in a regional hospital (Prince of Wales Hospital) over a 21-month period from November 2004 to July 2006. Patients' data were retrieved from the hospital electronic clinical information system (Clinical Management System). Demographic data and clinical characteristics of patients were studied. The modes of stroke prevention treatment before and after stroke were included. The reasons why patients were not given warfarin as primary and secondary prophylaxis of stroke were investigated.
Results: A total of 102 admissions were recorded during the study period. Twenty-one (20.6%) patients of the studied population were originally on warfarin pre-stroke. On discharge, 35 (41.7%) patients out of 84 survivors were on warfarin treatment. The major reasons identified for not being treated with anticoagulation before stroke were increased risk of gastro-intestinal bleeding, history of intracerebral haemorrhage, risk of fall, paroxysmal AF, patient's choice, old age, and unknown reasons or not offered by physicians. After stroke the main reasons for not being treated with anticoagulation were dependency and risk of fall, which both could be a consequence of stroke. Further statistical analysis showed that warfarin treatment was more likely associated with younger age-group, recurrent strokes, lacunar stroke or large artery disease, lower National Institute of Health Stroke Scale score on admission and discharging home post-stroke. However, it was not associated with higher CHADS2 score*, ie those patients with higher stroke risks.
Conclusions: Among acute ischaemic stroke patients with non-valvular AF admitted to acute stroke unit of a regional hospital, percentage prescription rate of anticoagulant was almost double as compared with pre-admission rate, but overall still less than half of indicated patients. Identified reasons for non-prescription of anticoagulant included risks of bleeding, physical disability, and advanced age. Potential targets to improve the treatment rate would be to further investigate for reasons why physicians not offer anticoagulation when it was indicated, and to explore the reasons why patients tend to refuse anticoagulation even when it was indicated.

* CHADS2: Congestive heart failure, Hypertension, Age ≥75, Diabetes mellitus, prior Stroke or transient ischaemic attack Risk Stratification Scheme

D 3

Valvular Heart Disease and Use of Bromocriptine in Patients with Parkinson's Disease

Chun-pong Chung
Department of Medicine, Queen Mary Hospital, Hong Kong

Background: Some ergot-derived dopamine receptor agonists used in treatment of Parkinson's disease, such as pergolide and cabergoline, have been demonstrated to be associated with increased risk of valvular heart disease. However, there were only few data available on the relationship between risk of cardiac valvular disease and bromocriptine, which was also an ergot-derived dopamine receptor agonist and was widely used in our locality for treatment of Parkinson's disease. The purpose of this study was to investigate the risk of cardiac valvulopathy in Parkinson's disease patients treated with bromocriptine.
Methods: Echocardiogram were performed in 62 patients with Parkinson's disease treated with bromocriptine for at least 1 year (bromocriptine group) and in 24 control subjects, which consisted of patients with Parkinson's disease who have never been exposed to any dopamine agonist (control group). Valve regurgitation was assessed according to American Society of Echocardiography recommendations. The mitral-valve tenting area was also measured and used as a quantitative index for leaflet stiffening. Patients in the bromocriptine group and control group were then compared.
Results: There was no significant difference between bromocriptine and control group in prevalence of regurgitation at mitral, aortic, and tricuspid valves. The odds ratio of the bromocriptine for moderate-to-severe (grade 3 or 4) regurgitation of any valve and for leaflet thickening of any valve according to the logistic regression analysis adjusted by age and sex were 0.69 (95% CI, 0.15-3.13; P=0.63) and 0.60 (95% CI, 0.21-1.70; P=0.33), respectively. Also, no significance difference between the bromocriptine and the control groups in terms of the mitral value tenting (3.57 ± 0.59 cm^2 vs 3.64 ± 0.59 cm^2, P=0.78) was detected. A weak but significant linear relationship (r=0.27, P=0.035) was observed between the cumulative dose of bromocriptine and the tenting area of mitral valve.
Conclusion: There was no increase in risk of developing cardiac valvular disease in Parkinson's disease patients at reasonable cumulative dose and duration of bromocriptine therapy. Unlike pergolide, it was safe to use bromocriptine to treat the patients with young-onset Parkinson's disease as far as the risk of cardiac valvulopathy was concerned.

D 4

Utility of Specific Cerebral Angiographic Features in Distinguishing Reversible Cerebral Vasoconstriction Syndromes from Primary Angiitis of the Central Nervous System

Joshua W Fok
Department of Medicine, Yan Chai Hospital, Hong Kong

Background: Primary angiitis of the central nervous system (PACNS) is a rare, inflammatory disorder of cerebral arteries resulting in stroke and progressive disability. Reversible cerebral vasoconstriction syndrome (RCVS) is an increasingly well-recognised syndrome that mimics PACNS due to overlapping features such as headache, stroke, and angiographic abnormalities. Historically, some patients with RCVS had been misinterpreted as PACNS and were subjected to the risks of brain biopsy and chronic immunosuppressive therapy. We hypothesised that there are distinctive cerebral angiographic features in RCVS and PACNS as a result of different underlying pathophysiology, namely inflammation in PACNS and vasospasm in RCVS.

Methods: Using ICD code 437.4 (cerebral vasculitis) and a keyword search of a neuroradiology database in Massachusetts General Hospital, 549 patients were identified with 'possible' cerebral vasculitis. Medical records were reviewed in detail. Thirty-five cases of 'definite' PACNS were diagnosed on basis of positive brain biopsy, or consistent clinical course along with inflammatory cerebrospinal fluid (CSF) and/or cerebral angiographic abnormalities. The RCVS group (n=81) was comprised of a series of 74 consecutive cases diagnosed by Dr Aneesh B Singhal in the Massachusetts General Hospital since 1997 and seven additional cases identified from the above search; all cases met diagnostic criteria for RCVS. The first cerebral angiogram after symptom onset (digital subtraction angiography [DSA] or computed tomographic angiography [CTA]) was available in 20 PACNS cases and 52 RCVS cases. Two investigators (Drs Aneesh B Singhal and Raul G Nogueira) who remained blinded to the diagnoses reviewed the angiographic images in random order and rated pre-defined angiographic features, namely severity, location, symmetry, and visual appearance of the affected segments.

Results: In the RCVS group (mean age, 44 years; 92% women), 88% had thunderclap headache at onset. In the PACNS group (mean age, 47 years; 20% women), 5% had thunderclap headache at onset, 74% had abnormal CSF and normal angiography in 15%. Patients with PACNS had poorer outcome (mRS=3) as compared to RCVS (mRS=1). The RCVS group (versus PACNS group) had a higher percentage of angiograms showing 'sausage on a string' appearance (83% vs 15%, P<0.001), more arterial segments with abnormal dilatation (67% vs 15%, P<0.001), and more arterial segments with severe narrowing (44% vs 34%, P=0.001). The characteristic 'sausage on a string' appearance had a high sensitivity (83%) and specificity (85%) for RCVS. Patients with PACNS showed a higher incidence of irregularly 'notched' arteries (70% vs 13%, P<0.001); this feature had a sensitivity of 70% and specificity of 87% for PACNS.

Conclusion: In patients with overlapping clinical features of RCVS and PACNS, cerebral angiographic findings of symmetric, segmental, 'sausage on a string' appearance (historically associated with PACNS) appears to be diagnostic of RCVS, whereas an irregular, 'notched' appearance points to the diagnosis of PACNS.

BAD: the Missing Link

D 5

May WM Kwan
Neurodiagnostic Unit, Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong

Background and purpose: Clinicians and researchers often classify atherosclerotic cerebral infarctions into: (1) large artery atherothrombotic disease (LAD), and (2) small artery lacunar infarction (LACI), but this system of dichotomisation cannot account for a substantial proportion of stroke cases. Hence, Caplan proposed the existence of a third mechanism for cerebral infarction—branch artery disease (BAD). However, this concept is understudied and underused, and BAD remains an obscure entity.
Methods: Stroke patients admitted under the Neurology Unit of a teaching hospital over a 24-month period were studied retrospectively. Patients with ischaemic stroke presumably due to atherosclerotic disease were classified according to their imaging and/or clinical findings into three groups: LAD, BAD, and LACI. Patients with BAD were further categorised into six BAD stroke syndromes based on radiological criteria. Clinical characteristics, vascular risk factors, results of vascular workup and outcome among the various stroke subgroups were compared.
Results: A total of 720 patients with a diagnosis of stroke were admitted during the study period, including 123 LAD (17% of all stroke cases or 33% of all studied patients), 155 BAD (22% or 42%), and 95 LACI (13% or 25%). Among the BAD patients, the number of cases involving Heubner's artery, lenticulostriatal arteries, anterior choroidal artery, thalamoperforating/geniculate arteries, paramedian pontine infarction, or non-hypertensive lacunar infarction were 0, 47, 45, 15, 40, or 8 (0%, 30%, 29%, 10%, 26%, or 5%), respectively. Patients with BAD were the youngest among the three groups. As compared to LAD patients, BAD patients had lower NIHSS score, were less often diabetic and carotid stenosis was less common, while stenosis of the intracranial arteries were more frequently seen in BAD as compared with LACI patients. The outcome of BAD patients was intermediate between LAD and LACI and the former had the worst outcome. Comparison of variables among the BAD stroke syndromes showed that they were a homogenous group of conditions.
Conclusions: Branch artery disease–associated cerebral infarction is a prevalent subtype of ischaemic stroke, and the homogeneity among the BAD stroke syndromes suggests it might represent a distinctive stroke entity. Although patients with BAD and LACI had similar degrees of neurological deficits on presentation, outcome in the former group was significantly worse than the latter.

Clinically Isolated Syndrome in Hong Kong and Long-term Outcomes

D 6

Richard Li
Pamela Youde Nethersole Eastern Hospital, Hong Kong

Objective: The data on clinical isolated syndrome and its relationship to multiple sclerosis in the Chinese population is not well studied. This study aimed to retrospectively study the clinical and radiological profile of a prospective cohort of patients with clinically isolated syndrome (CIS), the rate of conversion to clinically definite multiple sclerosis (CDMS), the associated risk factors, and the long-term outcomes.
Methods: From May 1997 to April 2007, 68 CIS patients presented to our hospital were enrolled in a registry and all were offered long-term follow-up by our department. Their clinical characteristics, baseline MRI brain and spine findings (performed within 3 months after symptom onset) and investigations were systematically recorded in the registry. The outcomes and most updated status as at May 2009 of all patients were ascertained by review of hospital records, retrieval of information from the Clinical Management System of the Hospital Authority and telephone follow-up by the author if necessary. The data collected were then critically analysed to determine the median time and rate of conversion to CDMS, the associated risk factors and development of disability. Kaplan-Meier analysis was used to estimate the probability of conversion to CDMS in different MRI subgroups classified by the Barkhof/Tintoré criteria.
Results: Multiple sclerosis developed in 29 (42.6%) patients after a mean follow-up of 64.6 months. Younger age of onset, CIS presentation as brainstem/hemispheric syndrome and abnormal baseline MRI were significantly correlated with conversion to CDMS ($P<0.05$). The median time of conversion to CDMS was 11.5 months for patients developed multiple sclerosis at the time of this review. Patients fulfilling dissemination in space (DIS) according to the Barkhof/Tintoré criteria in baseline MRI brain had 80% probability to develop the second neurological event to qualify CDMS within 2 years. Overall, the cumulative probability of conversion to CDMS of the patients with abnormal MRI brain was 50% in 2 years. Patients developed multiple sclerosis would have 50% probability to reach Expanded Disability Status Scale (EDSS) >3.0 in 18 months.
Conclusions: Local CIS patients have similar risk profile to Caucasian patients in converting to CDMS. The Barkhof/Tintoré DIS criteria are applicable to local CIS population. The magnitude of fulfilment of the Barkhof/Tintoré criteria is useful in risk stratification for local CIS patients and carries important prognostic value. The CDMS patients were more disabled than those monophasic CIS patients and accumulation of disability was fast.

D 7

Aspirin Failure in Non-cardioembolic Ischaemic Stroke: a Retrospective Cohort Study on Its Incidence, Choice of Antiplatelet Treatment, and Clinical Outcome

Alan CT Tse
Division of Neurology, Department of Medicine, Queen Mary Hospital, Hong Kong

Background: Aspirin plays a central role in the secondary prevention of ischaemic stroke and other vascular events in stroke patients. When a vascular event recurs despite aspirin, the optimal antiplatelet treatment and the clinical outcome are unknown.
Objectives: To determine the incidence of aspirin users who presented with acute non-cardioembolic ischaemic stroke in Hong Kong, to address the choice of antiplatelet drug(s) afterwards, to observe the respective clinical outcome under different treatments, and to evaluate possible factors that may account for any observed difference in the outcomes.
Methods: This is a retrospective observational cohort study carried out in a teaching hospital. Patient records were retrieved from our Stroke Registry over a 4-year period between 2004 and 2007. Patients who presented with non-cardioembolic stroke with prior aspirin consumption for at least 7 days were recruited. The choices of antiplatelet treatment and the clinical outcomes were collected from Clinical Management System and by telephone interviews when necessary. The primary outcome was a composite of non-fatal ischaemic stroke, non-fatal myocardial infarction and vascular death. The secondary outcomes included vascular and non-vascular death and any bleeding complications.
Results: A total of 334 patients were included into the study. The incidence of clinical aspirin failure (CAF) in non-cardioembolic stroke patients was 89.5 cases per year, or 13.5% of all non-cardioembolic strokes. A total of 214 (64.1%) patients had chosen to keep original dose of aspirin ('Keep'), 69 (20.7%) patients had increased the dose of aspirin ('Increase'), and 48 (14.4%) patients had either used an alternative antiplatelet drug or a combination of them ('Others'). For a mean follow-up interval of 39.3 months, no statistically significant difference was observed in the primary outcome (31.3% in 'Keep' vs 33.3% in 'Increase' vs 21.6% in 'Others'; P=0.325) among the three groups. For all-cause mortality, there was a trend towards lower death rate in 'Increase' group (20.3% in 'Increase' vs 35.5% in 'Keep' vs 29.4% in 'Others'; P=0.057). There was no difference in bleeding complications (16.8% in 'Keep' vs 14.5% in 'Increase' vs 21.6% in 'Others'; P=0.588).
Conclusion: Clinical aspirin failure in ischaemic stroke patients is a common clinical entity among the Hong Kong Chinese population. In comparison with aspirin continuation, no significant extra benefits were demonstrated with the use of a higher dose of aspirin, an alternative antiplatelet or a combination therapy in this cohort of patients.

Central Nervous System Lymphoma—Clinical, CT and MR Correlation

P 1

KY Lau[1], EMW Man[1], WWC Wong[1], SSW Lo[1], JLS Khoo[1], JKW Chan[1], TH Tsoi[2]
[1] Department of Radiology, Pamela Youde Nethersole Eastern Hospital, Hong Kong
[2] Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong

Objective: Central nervous system (CNS) lymphoma is not common. Primary CNS lymphomas represent 1% of all lymphomas and as many as 16% of all primary brain tumours. In 5 to 9% of systemic non-Hodgkin's lymphoma, secondary spread involves the CNS. However, with an increasing incidence in both the immunocompetent and immunocompromised populations, this amplified prevalence makes CNS lymphoma an important consideration in the differential diagnosis of brain lesions. The CT and MRI findings of intracranial lymphomas can be non-specific. Radiologists should be aware of the imaging features to make a prompt diagnosis and hence give treatment.
Methods: From 2000 to 2008, 13 patients with histological proven CNS lymphoma were retrospectively reviewed. The clinical presentation, CT and MR findings were correlated.
Results: Among 13 patients, there were seven males and six females. Their ages ranged from 32 to 83 (mean, 62.5) years. Primary CNS lymphoma was noted in 11 and secondary CNS lymphoma in 2 patients. Among 11 primary CNS lymphomas, 3 patients presented with headache only, 1 headache and unsteady gait, 2 hemiparesis, 3 dizziness and syncope, 1 facial and tongue numbness, 1 diplopia. For two patients with secondary CNS lymphoma, one presented with intestinal obstruction and 1 tonsilar involvement. None of these patients were suffering from AIDS nor immunocompromised. All had CT and MR of the brain performed. Their CT and MR findings will be correlated and presented.
Conclusion: The clinical presentation, CT and MR findings are bizarre and non-specific. High index of suspicion with clinical and imaging correlation are essential to make a prompt diagnosis and guide management.

Pilot Project of Integration of Chinese Medicine (Acupuncture) and Western Medicine for Neurohabilitation of Children with Acquired Brain Injury—a Study of Two Cases

P 2

Virginia CN Wong[1], L Li[2], SS Lam[2], CL Wong[1], Vanessa Chu[1]; Neurohabilitation Team of Duchess of Kent Children Habilitation Institute
[1] Department of Paediatrics and Adolescent medicine, Faculty of Medicine, The University of Hong Kong, Hong Kong
[2] School of Chinese Medicine, Faculty of Medicine, The University of Hong Kong, Hong Kong
[3] Duchess of Kent Children Habilitation Institute, Hong Kong

Purpose: To demonstrate if there is any efficacy of integration of Chinese medicine (acupuncture) and western medicine for rehabilitation for two children with acquired brain injury (ABI).
Methods: Two children (M/1 year, with dystonic cerebral palsy, cortical visual impairment and global developmental delay due to acute encephalitis; and M/12 years, with spastic tetraplegia, cortical visual impairment, and severe mental retardation due to hypoxic-ischaemic encephalopathy related to hypertrophic cardiomyopathy) were enrolled into our pilot programme which had started as the 'First Integrated Chinese Medicine and Western Medicine for Neurorehabilitation of Children with Traumatic or Acquired Brain Injury under the Hospital Authority' in June 2008. Both of them received daily acupuncture treatment and conventional neurohabilitation programme for 4 months. Pre- and post-assessment were performed for both cases. Deoxyglucose PET scan of the brain, parental daily reports for any change after each acupuncture session were monitored. Objective outcome measures were performed by the Neurohabilitation Team with allied health disciplines including physiotherapist, occupational therapist, optometrist, audiologist, speech therapist and clinical psychologist in pre- and post-acupuncture treatment using objective outcome measures including Modified Ashworth Spasticity Scale, CVI assessment, Video Fluoroscopic Swallow Study (VFSS) and Functional Independence Measure of Children (WeeFIM). Videos were taken by blind assessors.
Results: PET scan of the brain showed mild-to-moderate increase in glucose uptake for both cases. Videos and clinical outcome measures showed improvement in vision and other parameters.
Conclusions: A short and intensive course of acupuncture can be effective in improving visual and functional outcome for children with ABI. Further research is underway to assess the practicability of organising this model of integration of Chinese medicine (acupuncture) and western medicine for neurohabilitation of children with ABI in Hong Kong.

Reasons for A&E Consultation and Hospital Admission for Parkinson's Disease

P 3

HF Chan[1], YF Cheung[1], WC Fong[1], KW Fong[1], LT Chan[1], YC Chan[1], WT Lo[1], HF Ho[2], HM Chan[1], CK Li[1]
[1] Division of Neurology, Department of Medicine, Queen Elizabeth Hospital, Hong Kong
[2] Department of Accident and Emergency, Queen Elizabeth Hospital, Hong Kong

Background: Parkinson's disease (PD) patients have various reasons to consult the Accident and Emergency Department (A&E) which may lead to hospital admission. Better understanding of these reasons may help design preventive measures to reduce A&E attendance and hospitalisation.
Methods: We conducted a retrospective review on patients with ICD9CM Codes of "Paralysis agitans", "Parkinson's disease" or "Parkinsonism—atherosclerotic, idiopathic or primary" on or before attendance between 27 June 2008 and 26 June 2009 in the Specialist Outpatient Clinic of Queen Elizabeth Hospital. Reasons for A&E attendance and hospital admission between 1 July 2006 and 30 June 2009 and patients' characteristics were determined for randomly selected patients.
Results: A total of 457 patients were retrieved. We randomly selected 50 patients, 47 out of 50 had PD who fulfilled the Queen Square Brain Bank (QSBB) criteria; 55% were male. The median age was 68 (range, 50-86) years. They had their diagnosis at the median age of 61.5 (range, 41-82) years, and a mean disease duration of 5.8 (range, 2.1-18.5) years. These patients paid 92 (range, 0-15) visits to the A&E at the selected period (0.65 visits per patient per year); 21 (44.7%) patients did not visit A&E at all. The reasons for A&E consultations were motor symptoms (7.6%), psychiatric or cognitive symptoms (7.6%), falls (21.7%; 20% of these falls were complicated by fractures), infection (9.8%), gastro-intestinal especially constipation (14%), hypotension (1%), deep brain stimulation related (1%), cardiovascular (3.3%), musculoskeletal (12%) and miscellaneous (21.7%). Thirty-six (39%) of A&E attendance led to hospitalisation and 20 were PD-related symptoms (ie excluding musculoskeletal, cardiovascular, and miscellaneous causes). The mean length of stay was 8.49 and 8.41 days respectively for overall and PD-related symptoms. No mortality was found.
Conclusion: Fall is the leading cause of A&E visit in our PD patients. A significant proportion can result in fractures and immobility. This problem, however, can be avoided by early intervention. Therefore, further studies are warranted for better evaluation in this area in order to reduce unnecessary admission and morbidities.

Median-ulnar Mixed Nerve Latency Difference to the Mid-palm in Carpal Tunnel Syndrome

P 4

Kwai-fu Ko[1], Kwai-ping Yiu[1], Wing-yan Lau[1], Wing-keung Cheng[1], Min-chung Kwan[1], Tsz-pang Chan[2]
[1] Department of Medicine and Geriatrics, Kwong Wah Hospital, Hong Kong
[2] DREC, Wong Tai Sin Hospital, Hong Kong

Background: A sensitive method for electrophysiological testing of carpal tunnel syndrome is warranted. It will help to clinch the diagnosis, especially in those patients with negative physical signs and facilitate early diagnosis, thereby preventing the occurrence of excessive wallerian degeneration.
Methods: A total of 106 subjects (age range, 22-77 years; mean age, 53.9 years) with clinically suspected carpal tunnel syndrome were studied in the Electro-diagnostic Unit of Kwong Wah Hospital by the same neurologist. Median motor latency, median motor conduction velocity, and sensory nerve conduction velocity were evaluated using the traditional methods. The wrist-palm mixed nerve latency differences between the median and ulnar nerves were measured.
Results: The sensitivity of the median motor distal latency was 68.4%. The sensitivity of the median sensory conduction method was much higher and was 95.9%. The comparison of median to ulnar mixed nerve conduction from palm to wrist was able to detect abnormalities in four hands out of three patients with carpal tunnel syndrome who would be otherwise regarded as normal if merely assessed by the traditional electrophysiological methods.
Conclusion: Median-ulnar mixed nerve latency difference to the mid-palm facilitates diagnosis of patients with carpal tunnel syndrome.

Diffusion-weighted MR imaging of Creutzfeldt-Jakob Disease

P 5

R Lee[1], HK Chan[2], SYY Pang[2], SFK Hon[2], W Mak[2], RTF Cheung[2], SL Ho[2], KS Tai[1]
[1] Department of Radiology, Queen Mary Hospital, Hong Kong
[2] Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Two consecutive cases of probable sporadic Creutzfeldt-Jakob disease (CJD) were diagnosed in year 2008. They both presented with progressive dementia with moderate-to-severe cognitive impairment at the time of presentation to our institution. The Mini-Mental State Examination scores were 12 and 13 out of 30. Magnetic resonance imaging (MRI) and magnetic resonance angiography was performed for both patients. Both patients showed cortical grey matter lesions without any involvement of the deep grey nuclei, particularly the caudate nuclei. The cortical grey matter showed subtle increase in signals on T2-weighted MRIs with restricted diffusion. No particular MR signal change could be seen on the T1-weighted images, fluid-attenuated inversion recovery (FLAIR) images or the post-gadolinium contrast enhanced images.

Subsequent electroencephalogram showed characteristic periodic synchronous discharges. Clinically, myoclonus and extra-pyramidal signs were more obvious in subsequent follow-up of the patients.

Early recognition of this deadly condition is crucial as human-to-human transmission is possible and should be prevented by all means; especially when we are in an era of organ transplant.

Paediatric Epilepsy Surgery Programme in Hong Kong—Experience in Queen Mary Hospital/Duchess of Kent Children's Hospital

P 6

Ada WY Yung[1], Virginia CN Wong[1], Pek L Khong[2], Henry Mak[2], KN Hung[3], PH Chan[3], WY Ho[4], YW Fan[3]
[1] Division of Child Neurology/Developmental Paediatrics/Neurohabilitation, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital/Duchess of Kent Children's Hospital, The University of Hong Kong, Hong Kong
[2] Department of Radiology, University of Hong Kong, Hong Kong
[3] Department of Neurosurgery, Queen Mary Hospital, Hong Kong
[4] Department of Diagnostic radiology, Queen Mary Hospital, Hong Kong

Background: Surgery is a well-established treatment for adults with intractable seizures. Increasingly, infants and children are being considered for epilepsy surgery. In a growing child, epilepsy surgery has the additional benefit of aborting cognitive decline and improving development and behaviour.

Methods: The paediatric epilepsy surgery programme as well as paediatric video telemetry service were set up in Queen Mary Hospital since the early 1990s. From 1998 to 2006, a total of 10 patients were sent overseas for resective surgery. One patient suffered from Rasmussen's syndrome, three patients with tuberous sclerosis, three with focal cortical dysplasia, three with hypothalamic hamartoma. Since 2001, regular epilepsy surgery joint clinic was set up. From 2002 till now, 14 patients underwent curative epilepsy surgery at our centre. One patient suffered from Rasmussen's syndrome, three patients with multi-lobar cortical dysplasia, four patients with focal cortical dysplasia, one with tuberous sclerosis, two with dysembryoplastic neuroepithelial tumour, one with gliosis, two with mesial temporal sclerosis.

Results: Age at operation ranged from 3 months to 19 years. Age from seizure onset to surgery ranged from 2 months to 16 years. Seizure outcome at a mean of 3.5 years long-term follow-up (3 months-7 years), using Engel's classification, was class 1 in five (36%) patients, class II in 5 (43%) patients, and class III in 3 (21%) patients.

Conclusion: With careful case selection, early surgical intervention in paediatric patients with intractable epilepsy is associated with favourable outcome and provides an important opportunity in preventing irreversible decline in intelligence and disability.

P 7

Risk Factors Associated with Refractory Epilepsy in Children—The University of Hong Kong Experience

Virginia CN Wong, Ada WY Yung
Division of Child Neurology/Developmental Paediatrics/Neurohabilitation, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital/Duchess of Kent Children's Hospital, The University of Hong Kong, Hong Kong

Background: There is a lack of consensus about the definition of intractable or refractory epilepsy in children. Medically intractable epilepsy occurred in 10 to 20% of epilepsy with childhood onset. Patients with medical intractability had immense resource implication and lifelong disability/disabilities. Early identification of risk factors for refractory epilepsy offers a chance of appropriate and timely treatment thus affecting prognosis.
Methods: A retrospective study was performed for our cohort of 505 children aged below 18 years with new-onset epilepsy, diagnosed between 1979 and 2006, and actively managed at the Comprehensive Epilepsy Clinic, Department of Paediatrics and Adolescent Medicine of the University of Hong Kong. We arbitrarily defined refractory epilepsy as those who had never been seizure-free for more than 12 months despite receiving anti-epileptic drug (AED) treatment. Responders were arbitrarily defined as those who had at least been seizure-free for consecutive 12 months. All patients had been on one or more AEDs and were followed up for at least 24 months after AED initiation. The demographic, clinical, diagnostic, investigative, management and seizure outcome at 2 years were analysed.
Results: At 2 years' follow up, 42% (n=212) had refractory epilepsy. Risk factors significantly correlated with refractory epilepsy included history of status epilepticus (P<0.001), symptomatic aetiology (P<0.001), use of two or more AEDs (P=0.001), abnormal neurological co-morbidities including mental retardation (IQ<70) [P<0.001], learning disabilities (IQ=70-90) [P=0.009], cerebral palsy (P=0.011), abnormalities in EEG (P<0.001) and neuroimaging (P<0.001).
Conclusions: Early identification of risk factors to predict possible medical intractability is important in improving treatment strategies especially in the selection of traditional versus newer AEDs, mono- versus poly-pharmacy or even earlier alternative epilepsy management decision plans including evaluation for possible surgical therapies.

P 8

Posterior Reversible Encephalopathy Syndrome: Paediatric Heart Transplant with Cyclosporine Neurotoxicity

W Tso[1], AWY Yung[1], KS Lun[2], TC Yung[2], K Fan[3], VCN Wong[1]
[1] Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[2] Department of Paediatric Cardiology, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[3] Department of Cardiology, Grantham Hospital, Hong Kong

Posterior reversible encephalopathy syndrome (PRES) is associated with a specific disorder of cerebrovascular autoregulation. Clinical features of PRES consisted of headache, decreased consciousness, altered mental functioning, seizures, visual loss or cortical blindness. Characteristic findings on neuroimaging included high signal intensity on T2-weighted as well as diffusion-weighted imaging MRI in the posterior cerebral hemispheres, indicative of vasogenic subcortical oedema without infarction. Cyclosporine neurotoxicity had been described following bone marrow and organ transplantation; however, there are few reports of PRES in children especially post-paediatric heart transplantation. We report a case of cyclosporine-related PRES in a paediatric heart transplant recipient. She made a good recovery with no residual neurological deficits after withdrawal of cyclosporine, control of possible risk factors as well as symptomatic control of seizure.

P 9

Electro-acupuncture for Children with Autism Spectrum Disorder: Pilot Study of Two Cases

WX Chen[1], WL Liu[2], VCN Wong[1]
[1] Division of Child Neurology/Developmental Paediatrics/Neurohabilitation, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[2] Tung Wah Group of Hospitals, Clinical Centre for Teaching and Research in Chinese Medicine, The University of Hong Kong, Hong Kong

Objective: To observe for efficacy, safety, and compliance of electro-acupuncture for autism spectrum disorder (ASD).
Methods: Two children with ASD received electro-acupuncture for 24 sessions over 8 weeks and were assessed pre- and post-acupuncture. We defined a positive or negative change as an improvement or deterioration of 25% respectively in total score or any subscales of Aberrant Behavioral Checklist (ABC), Ritvo-Freeman Real Life Scale (RFRLS), WeeFIM, and as a rating of much improved or much worse on the Clinical Global Impression–Improvement (CGI-I) scale.
Results: For ABC, positive changes in 'Irritability' and 'Stereotypy' were noted in Case 1 but no changes occurred for Case 2. For RFRLS, positive changes were found for both cases in 'Sensory motor', 'Sensory response' and 'Total score', although negative change was noted for Case 2 in 'Affectual response"'. For WeeFIM, there were no positive or negative changes in both cases. For CGI-I, positive change in Case 1 with much improvement in 'Social relatedness, Communication and Stereotypy behaviour' was reported.
Conclusion: A short intensive course of electro-acupuncture might improve some core features of children with ASD.

Acupuncture for Autistic Spectrum Disorder

P 10

DKL Cheuk, VCN Wong, WX Chen
Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

Objectives: The objectives of this Cochrane systematic review were to determine the efficacy and safety of acupuncture therapy in patients with autism spectrum disorder (ASD). We intend to review whether acupuncture is effective in improving social, communication, behavioural impairment, quality of life and overall functioning, and whether acupuncture is associated with any adverse effects.
Methods: We searched the Cochrane Developmental, Psychosocial and Learning Problems Group (July 2009), the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 3, 2009), MEDLINE, EMBASE, PsycINFO, CINAHL, AMED, Dissertation Abstracts International, Cochrane CM Field Trials Register, NCCAM, NIH Clinical Trials Database. We also searched TCMLARS, China Biological Medicine Database, China Journal and Doctor Dissertation Full-text Database, China Proceeding Conference Database, Chinese Acupuncture Trials Register, and Index to Chinese periodical literature on WWW (tw). The proceedings of relevant conferences and the reference lists from relevant trials were reviewed. No language restrictions were imposed. Selection criteria were: randomised controlled clinical trials using random or quasi-random allocation of treatment. Studies comparing acupuncture with at least one control group that uses no treatment, placebo treatment or sham treatment were included.
Results: Six trials studied autistic children met the inclusion criteria, with four studies in Hong Kong, one each in mainland China and in Egypt. Meta-analysis was not done in three trials (Chinese trial, one of Hong Kong trials and Egyptian trial), which compared acupuncture with no acupuncture, due to the heterogeneity of outcome measures, although the improvement of autistic behaviour (Chinese trial) or language development (Egyptian trial) or overall functioning (Hong Kong trial) was reported respectively. In contrast, meta-analysis was performed in the remaining three Hong Kong studies, comparing acupuncture with sham acupuncture. Two trials showed a significant beneficial effect of tongue acupuncture in achieving overall functioning (weighted mean difference [WMD]=4.39; 95% CI, 2.85-5.92), self-care (WMD=3.63; 95% CI, 2.01-5.26), cognition (WMD=1.18; 95% CI, 0.37-1.99), comprehension language age (WMD=0.16; 95% CI, 0.03-0.29) and language age (WMD=2.08; 95% CI, 0.11-4.04), while another Hong Kong trial found a positive effect of body electro-acupuncture in improving language comprehension, self-care assistance and clinical global impression of children with ASD. Regarding the effect of acupuncture, all three remaining Hong Kong trials (two tongue acupuncture trials and one body electro-acupuncture trial) showed a significantly favourable effects in ameliorating overall functioning (WMD=3.69; 95% CI, 2.33-5.06), self-care (2.41; 95% CI, 1.16-3.65), cognition (WMD=0.87; 95% CI, 0.27-1.47), comprehension language age (WMD=0.15; 95% CI, 0.03-0.26) and language age (WMD=1.34; –0.02 to 2.69). A mild positive effect of acupuncture on autistic behaviour (WMD= –0.09; 95% CI, –0.09 to 0.03 [RFRLS] and WMD= –5.02; 95% CI, –11.51 to 1.48 [ATEC]) was also found, though not reaching statistical significance. Chinese trial was of low quality without adequate description of randomisation method, concealment of randomisation or blinding. On the other hand, either Chinese trial or Hong Kong and Egyptian trials were small trials with short follow-up.
Conclusions: Acupuncture might be useful as adjunctive to conventional western approach in improving functional aspects in children with ASD. Much larger high quality clinical trials with long-term follow-up are needed.

Calcium Channel Blockers Can Reduce Iron-induced Apoptosis in Neural Stem Cells

P 11

WX Chen, VCN Wong, M Yang, GCF Chan
Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

Excessive iron accumulation in the brain with oxidative damage has commonly been observed in haemorrhagic stroke as well as neurodegenerative disorders. It is partly mediated via extracellular signal–regulated kinases (ERK) signalling cascades that regulate a diverse neuronal functional processes including cell death. Since L-type calcium channels are key passages responsible for the iron entry into neuronal cells and therefore we postulated its blocker, nimodipine and flunarizine, could potentially protect against iron-induced neurotoxicity in neural stem cells (NSCs). In-vitro studies of iron overload on murine-derived multipotent neural stem cell line C17.2 cells and rat embryonic (E13.5) hippocampal neural stem cells (hNSCs) were performed. The cytotoxic effect of various forms of iron compound (ferrous ammonium sulfate, ferric chloride, and ferric ammonium citrate) on NSCs and the salvaging potential of calcium channel blockers (nimodipine and flunarizine) under such iron overloaded circumstances were studied. Cell viability was measured by XTT assay. Apoptotic cell death was assessed by annexin V/PI staining, activated caspase-3 and mitochondrial membrane potential (JC-1) using flow cytometry. The effect of iron overload on ERK activation as well as the rescuing effect of calcium channel blockers and MEK inhibitor (U0126) on ERK phosphorylation of iron-injured NSCs was also studied by flow cytometry. Our results showed that iron overload significantly decreased cell viability via inducing mitochondrial damage and caspase-3 activity in a dose- and time-dependent manner (0.15-1.8 mM, 24 and 48 hours). Clinically relevant doses of iron (0.6-0.9 mM) also induced ERK activation of NSCs. Under such conditions, calcium channel blockers could significantly improve cell viability by partially ameliorated iron induced apoptosis via preventing mitochondrial damage. Calcium channel blockers and U0126 also prevented ERK activation in iron-overloaded NSCs. In summary, iron-induced apoptosis of NSCs underwent mitochondria-mediated apoptotic pathway and it involved ERK activation. Calcium channel blockers could potentially protect iron-induced neurotoxicity in NSCs by inhibiting these processes.

Clinical Course of Patients with Myasthenia Gravis in Hong Kong

P 12

Eric SW Yeung, Chi-nam Lee, Richard Li, Sonny FK Hon, M Au-yeung, CM Cheung, TH Tsoi
Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong.

Background: With advances in treatment, the prognosis of patients with myasthenia gravis has much improved in western countries over the past decades. However there is a scarcity of local data.
Methods: We conducted a retrospective review of the patients with myasthenia gravis who had disease onset after 2000 and under our care. Patients were identified using keyword search for "myasthenia gravis" in the Clinical Data Analysis and Reporting System (CDARS). The demographic data, clinical characteristics and outcome were obtained from written medical records and the records in the Clinical Management System.
Results: A total of 88 patients were identified and included. Patients' mean age at onset was 54.2 years; 58 was female and 42 was male. Fifty-five (63%) had pure ocular symptoms, 23 (27%) with generalised myasthenia at onset, nine (10%) with ocular onset followed by secondary generalisation. A thymic abnormality was diagnosed by CT in 10 patients (9 thymoma, 1 hyperplasia). Thymectomy was performed in nine patients (5 for thymoma, 1 for hyperplasia, 3 for normal thymus). Prednisolone and azathioprine was used in 38.6% and 28% respectively, predominantly in generalised cases. Two refractory cases were treated with mycophenolate. Twenty-three patients experienced significant deterioration in myasthenic symptoms requiring hospitalisation, cumulating to 671 days of hospitalisation. Fourteen patients developed myasthenic crisis, and a total of 21 courses of intravenous immunoglobulin was given to them. Two patients did not respond to IVIg and required a total of seven courses of plasmapheresis. All-cause mortality was 9% (8/88) after an average follow-up of 5 years, with four deaths from each group. None were disease-related in the ocular group. Among the generalised group, two died of respiratory failure, one from severe sepsis. Overall disease-related mortality was 3.4%.
Conclusion: The outcomes of local myasthenia gravis patients are good and comparable with western countries.

A Girl with Atypical Chronic Inflammatory Demyelinating Polyneuropathy

P 13

Sophelia HS Chan[1], Windsor Mak[2], Virginia CN Wong[1]
[1] Division of Child Neurology/Developmental Paediatrics/NeuroHabilitation, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[2] Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a chronic, acquired immune and inflammatory disorder that targets the peripheral nerves. The cardinal features include a progressive or a relapsing-remitting course, predominant motor symptoms and signs, symmetrical involvement of arms and legs, proximal muscles involvement along with distal muscles, and decrease or absence of deep tendon reflexes. The diagnosis is confirmed by cerebrospinal fluid (CSF) protein elevation without pleocytosis, and nerve conduction evidence of a primary demyelinating polyneuropathy.

A 17-year-old girl was admitted with increase in falling and progressive difficulty in raising arms for 6 months. The weakness had a waxing and waning course for the past few months. One month before admission, she noticed diurnal variation of weakness with most severe weakness in the morning that usually got better in the afternoon. She complained of frequent shoulder pain, fluctuating limb weakness and chronic fatigability. Examination showed multiple sites of tenderness, neck and shoulder stiffness and fatigability. Rapid fluctuation of muscle weakness within the same day or within 1 to 2 days were observed. She was initially suspected to have fibromyalgia and she had slightly elevated erythrocyte sedimentation rate and positive for anti-dsDNA. Subsequent nerve conduction study confirmed demyelinating sensorimotor polyneuropathy with sparing of sural nerves. Lumbar puncture showed raised protein level and protein-cytological dissociation. MRI spine demonstrated gadolinium contrast enhanced nerve roots at the cauda equina. Chronic inflammatory demyelinating polyneuropathy was diagnosed. She was started on intravenous immunoglobulin with rapid clinical improvement.

Our patient demonstrated a close relationship between fibromyalgia and CIDP. The predominant presentation of fibromyalgia highlighting that neuropathic nature of pain and morning stiffness can be the atypical presentation at some stage of CIDP.

Anti-NMDA-R Encephalitis—an Encephalitis Lethargica-like Illness

P 14

Sophelia HS Chan[1], CW Fung[1], Ada WY Yung[1], SL Lee[1], Virginia CN Wong[1], Russell C Dale[2], Angela Vincent[3]
[1] Division of Child Neurology/Developmental Pediatrics/Neurohabilitation, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong
[2] Paediatrics and Child Health, Children's Hospital, Westmead, The University of Sydney, Australia
[3] Neuroimmunology Group, John Radcliffe Hospital; Department of Clinical Neurology, University of Oxford, United Kingdom

A girl of 3 years and 9 months with a 3-day history of fever and upper respiratory tract infection (URTI) was admitted with a generalised tonic-clonic convulsion, and delirium with screaming, non-sense talking, and agitation. For the first week after admission, she was lethargic with fluctuating awareness and mutism during the day but poor sleep at night. Workup for acute encephalopathy including autoimmune, infective, toxicology, metabolic and vasculitic screening showed negative findings. Erythrocyte sedimentation rate was markedly elevated and cerebrospinal fluid showed positive oligoclonal bands. Urgent MRI brain showed bilateral periventricular, multifocal hyperintense lesions on T2W and FLAIR images over the frontal, parietal and occipital regions without enhancement. Urgent electroencephalogram showed generalised slowing compatible with encephalopathic picture. Acute demyelinating encephalomyelopathy was initially suspected, and she was first given intravenous (IV) methylprednisolone, 30 mg/kg/day, for 5 days without evident response, and then IV immunoglobulin, 1 g/kg, for 2 days. After this treatment, there was some improvement in conscious level but the child remained mute. Repeated electroencephalogram showed improved slowing and sleep changes. In the second week, she developed dyskinesia with mouth chewing, tongue thrushing and finger rolling, and developed rigidity, dystonia and oculogyric crises. The dystonia caused mild rhadomyolysis with raised creatine kinase level. Encephalitis lethargica was suspected and L-dopa was started. After dose titration, she responded well to L-dopa at 1.5 mg/kg qid with improvement of dystonia and rigidity. At the third week, however, she developed recurrent generalised tonic-clonic convulsions. Phenytoin and sodium valproate were started. Repeated MRI brain confirmed increase hyperintensity and size of the previously demonstrated lesions (T2W and FLAIR images) with additional pons involvement, and evidence of cerebral atrophy. In view of both clinical and radiological evidences of active ongoing encephalitic process, a second course of IV immunoglobulin followed by methylprednisolone was given. After the second course of treatment, the child responded well with ongoing improvement. She regained full consciousness and remained seizure-free. After half a month of rehabilitation training, she could walk on her own recommenced full oral feeding. She remained mute, but had normal understanding for her age. Her speech gradually returned 2 months after onset of illness. As this girl has encephalitis lethargica-like illness, NMDA-R encephalitis was suspected. NMDA-R antibodies in both serum and cerebrospinal fluid confirmed raised titres. Ultrasonogram of pelvis was normal.

In summary, this 3-year-old girl who developed a post-URTI encephalopathy with neuropsychiatric presentation, movement disorder, mutism, sleep disorder and seizures, symmetrical white matter changes, improvement after IV immunoglobulins and steroids, has anti-NMDA-R encephalitis. Her clinical features were typical of anti-NMDA-receptor encephalitis[1] which is associated with antibodies against the NR1-NR2 heteromers of the NMDA receptor, and often ovarian tumours in young adult females. The same antibodies have been shown in children with 'encephalitis lethargica'.[2] Long-term follow-up and monitoring of antibody titres are important as relapse may occur in some of the affected patients. This is the first case of anti-NMDA receptor encephalitis reported in Hong Kong.

References

1. Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol 2008;7:1091-8.
2. Dale RC, Irani SR, Brilot F, et al. N-methyl-D-aspartate receptor antibodies in pediatric dyskinetic encephalitis lethargica. Ann Neurol. Epub 2009 July 20.

Suspected Herpes Simplex Encephalitis in a Regional Hospital

P 15

May WM Kwan
Neurodiagnostic Unit, Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong

Background: Herpes simplex encephalitis (HSE) is the commonest sporadic infective encephalitis in Hong Kong. Early recognition of HSE, which relies on a high index of suspicion, is important as effective treatment is available. Empirical acyclovir is advocated for all cases of clinically suspected viral encephalitis. Electroencephalography (EEG) is a routine investigation in suspected HSE.
Methods: The EEG database of Neurodiagnostic Unit, Queen Mary Hospital, was reviewed retrospectively. All referrals from April 2006 to March 2009 with a diagnosis of suspected HSE treated with empirical intravenous acyclovir were identified. Their presenting features, imaging and laboratory findings, and final diagnosis were studied.
Results: During the study period, 60 patients (mean age, 51; range, 18-90 years, M:F=13:7) underwent EEG for suspected HSE. Presenting features included fever (n=39), confusion (39), impaired consciousness (31), focal signs (15, seizure in 8), and headache (13). All patients underwent brain CT and 45 had MRI. The commonest imaging findings were unrelated old changes (20) and normal study (16). Lobar inflammation was detected in four patients. The EEG was normal, showed diffused abnormalities or focal/multifocal abnormalities in 16, 31 or 13 patients, respectively. Lumbar puncture was performed in 59 patients. Total cell count was $\leq 10 \times 10^6$ /L in 68% of patients and CSF protein was <0.8 g/L in 51% of patients. Polymerase chain reaction for herpes simplex virus was positive in one out of 56 requests. Viral encephalitis was the final diagnosis in three patients (HSE=1, Japanese encephalitis=1, other virus=1). Other common diagnoses included meningitis (9), non-CNS sepsis (9), psychiatric illness (8), epileptic seizure (6), and acute stroke (5).
Conclusions: Our findings demonstrate that we are exercising a high index of suspicion for diagnosing HSE. Our liberal use of empirical acyclovir is also consistent with the Infectious Diseases Society of America (IDSA) recommendations. Despite our low threshold of investigating for HSE, only one case was identified over 3 years, suggesting HSE is an uncommon condition.

AUTHOR INDEX

	Page No.
A	
L Au	27
M AuYeung	30, 45
B	
RJ Barohn	25, 26
C	
AYY Chan	27, 28, 30
B Chan	17, 18
DTM Chan	28
GCF Chan	45
HF Chan	33, 40
HK Chan	41
HM Chan	40
I Chan	22
JKW Chan	39
LT Chan	40
PH Chan	41
SHS Chan	46, 47
TP Chan	40
WX Chan	43
YC Chan	40
RCC Chang	11
JF Chao	11
C Chen	34
WX Chen	29, 44, 45
XY Chen	30
KM Cheng	18
WK Cheng	40
DKL Cheuk	44
CM Cheung	30, 45
PT Cheung	32
RTF Cheung	41
YF Cheung	40
V Chu	39
CP Chung	35
D	
RC Dale	47
F	
K Fan	42
YW Fan	41
JW Fok	36
KW Fong	40
WC Fong	40
CW Fung	32, 47
G	
DS Goodin	24
H	
G Halliday	14, 16
JH Han	30
HF Ho	40
P Ho	13
SL Ho	41
WY Ho	41
YS Ho	11
SFK Hon	30, 41, 45
V Hui	27
KN Hung	41

	Page No.
I	
V Ip	27
K	
PL Khong	41
JLS Khoo	39
JS Kim	17
KF Ko	40
MC Kwan	40
MWM Kwan	37, 48
P Kwan	22, 28
SY Kwan	22
A Kwok	32
B Kwok	19
JCK Kwok	18
L	
SS Lam	39
W Lam	29
AYL Lau	27, 28, 30
KK Lau	23
KY Lau	39
WY Lau	40
CN Lee	30, 45
R Lee	41
SL Lee	47
C Leung	27
H Leung	28, 30
KL Leung	28
T Leung	27, 29, 30
CK Li	40
L Li	39
R Li	30, 37, 45
WL Liu	29, 43
SSW Lo	39
WT Lo	40
L Low	32
WM Lui	18
KS Lun	42
M	
C Mak	32
H Mak	29, 41
W Mak	41, 46
EMW Man	39
Y Mizuno	12, 15
MYN Mok	30
N	
HK Ng	26
O	
TJ O'Brien	23
P	
KY Pang	18
SYY Pang	41
G Poon	32
S	
WC Shum	27
S Siu	32
YOY Soo	27, 29, 30

T
KS Tai 41
S Tam 32
CB Tan 18
D Treiman 20
ACT Tse 38
W Tso 42
TH Tsoi 30, 39, 45

V
A Vincent 47

W
MF Wang 11
CL Wong 39
E Wong 27, 30
LKS Wong 27, 28, 29, 30
VCN Wong 29, 31, 32, 39, 41, 42, 43, 44, 45, 46, 47
WWC Wong 39

X
L Xiong 30

Y
M Yang 45
ESW Yeung 30, 45
KP Yiu 40
S Yu 18, 29
AWY Yung 31, 41, 42, 47
KKL Yung 13
TC Yung 42

Z
CXL Zhu 28