SUPPLEMENT 7

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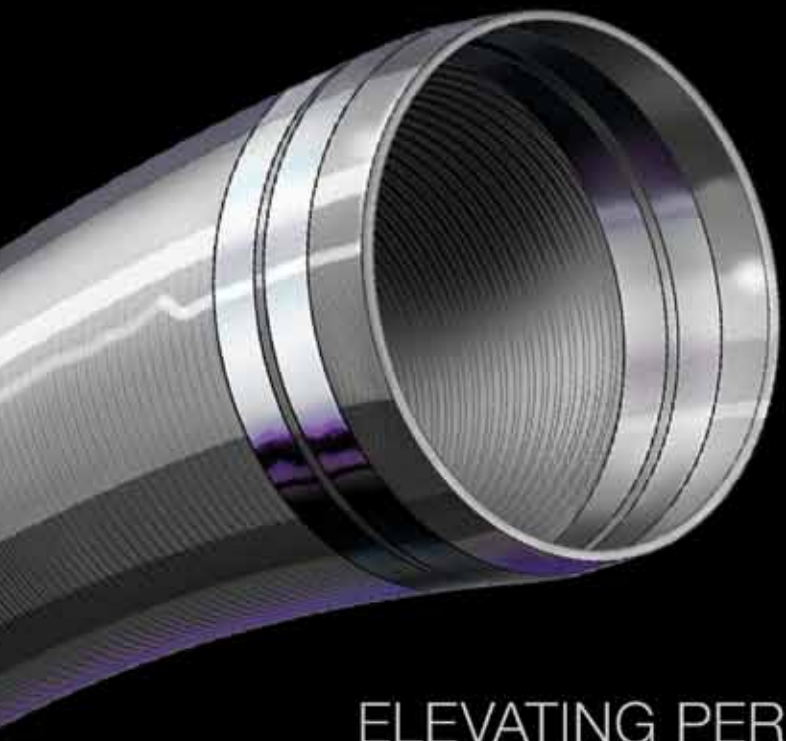

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31st Annual Scientific Meeting of The Hong Kong Neurological Society

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List of Speakers

Name	Affiliation
Prof Zohar Argov	Hadassah-Hebrew University Medical Center, Israel
Prof Nafi Aygun	Johns Hopkins University School of Medicine, USA
Prof Peter Alan Barber	Neurological Foundation of New Zealand, New Zealand
Prof Tanuja Chitnis	Harvard Medical School, USA
Prof Akio Ikeda	Kyoto University School of Medicine, Japan
Prof Tudor G Jovin	University of Pittsburgh School of Medical, USA
Prof Patrick Kwan	University of Melbourne, Australia
Prof Volker Limmroth	University of Cologne, Germany
Prof Zhongrong Miao	Beijing Tiantan Hospital, Capital Medical University, China
Dr Owen Tsang	Princess Margaret Hospital, Hong Kong SAR
Prof Anneke van der Walt	Monash University, Australia
Prof Lawrence KS Wong	The Chinese University of Hong Kong, Hong Kong SAR

Scientific Programme

Venue: Grand Ballroom, Level 3, JW Marriott Hotel, Admiralty, Hong Kong SAR

3 November 2018, Saturday

08:15 – 08:30	Registration	Function Room
08:30 – 10:00	**Education Session** Chairpersons: *Eric Chan, Betty Ng* **Magnetic resonance imaging sequences/techniques and their importance in diagnosis** *Nafi Aygun* **Pattern recognition in computed tomography / magnetic resonance imaging of the brain** *Nafi Aygun*	**Poster Presentation**
10:00 – 10:30	Coffee Break	
10:30 – 11:45	**Dissertation Highlights** Chairperson: *Bun Sheng* Judges: *SH Ng, Colin Lui*	
12:00 – 12:15	**Opening Ceremony**	
12:30 – 14:00	**Boehringer Lunch Symposium** Chairpersons: *Yannie Soo, Richard Li* **Breakthrough treatment in embolic stroke of undetermined source** *Lawrence KS Wong* **Answer the unanswered in secondary stroke prevention in atrial fibrillation population** *Peter Alan Barber*	
14:10 – 14:45	**Free Paper Presentation** Chairperson: *Bun Sheng* Judges: *Paul Chang, WC Fong, Winnie Wong*	
14:45 – 15:00	Coffee Break	
15:00 – 16:30	**Neuromuscular Disease Symposium** (co-organized with Hong Kong Society of Neuromuscular Diseases) Chairpersons: *Sophelia Chan, CN Lee* **Clinical diagnosis and management of hereditary myopathies in teenage and adulthood** *Zohar Argov* **Treatment of myasthenia gravis: from basics to advanced** *Zohar Argov*	

4 November 2018, Sunday

		Function Room
08:15 – 08:30	Registration	
08:30 – 09:15	**Sanofi Multiple Sclerosis Symposium** Chairpersons: *KL Shiu, WK Cheng* **Treatment of highly active relapsing-remitting multiple sclerosis** *Volker Limmroth*	**Poster Presentation**
09:15 – 10:00	**Novartis Multiple Sclerosis Symposium** Chairpersons: *KL Shiu, WK Cheng* **Management of paediatric multiple sclerosis: from adolescence to adulthood** *Tanuja Chitnis*	
10:00 – 10:15	Coffee Break / Poster Viewing Session Judges: *KK Lau, KY Cheung*	
10:15 – 11:45	**Synapse Stroke Symposium** (Co-organised with Hong Kong Stroke Society) Theme: *Mechanical thrombectomy in East and West* Chairpersons: *Thomas Leung, WC Fong* **A new DAWN in the treatment of acute ischaemic stroke** *Tudor Jovin* **Residual stenosis post-thrombectomy: an emerging challenge** *Zhongrong Miao*	
12:00 – 13:00	**Merck Lunch Symposium** Chairperson: *Jessica Li* **Immune reconstitution therapies in multiple sclerosis: the impact on treatment decision** *Anneke van der Walt*	
13:15 – 14:45	**Central Nervous System infection Symposium** Chairpersons: *KK Lau, Nelson Cheung* **Advances in neuroimaging in central nervous system infection/inflammation** *Nafi Aygun* **Central nervous system infection in immunocompromised patients** *Owen Tsang*	
14:45 – 15:00	Coffee Break	
15:00 – 16:30	**Eisai Epilepsy Symposium** Chairpersons: *Eric Chan, Jason Fong* **Diagnostic and therapeutic odyssey of epilepsy in the era of precision medicine** *Patrick Kwan* **Inflammation and epilepsy** *Akio Ikeda*	
16:30 – 16:40	Closing Ceremony and Award Presentations	

ES 1

Magnetic resonance imaging sequences/techniques and their importance in diagnosis

Nafi Aygun
Department of Radiology, Johns Hopkins University School of Medicine, USA

To review the basic magnetic resonance imaging pulse sequences and to discuss their strengths and weaknesses, to enhance the understanding of the impact of the selection of pulse sequence on clinical diagnosis, and to explore novel pulse sequences and their clinical use.

ES 2

Pattern recognition in computed tomography / magnetic resonance imaging of the brain

Nafi Aygun
Department of Radiology, Johns Hopkins University School of Medicine, USA

To differentiate neoplastic brain lesions from non-neoplastic ones, acute from chronic disease processes, and systemic/metabolic diseases from local/regional lesions.

DH 1

Factors predicting favourable outcome for decompressive hemicraniectomy in malignant middle cerebral artery infarction

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

Background: The mortality of malignant middle cerebral artery (MCA) infarction is about 80%. Decompressive hemicraniectomy has been suggested to decrease mortality and improve functional outcome. Nevertheless, it is unclear which groups of patients benefit most from this surgical intervention. The quality of life remains a key factor in decision making.
Aims: To explore factors associated with improved survival and favourable outcome after decompressive hemicraniectomy in patients with malignant MCA infarction.
Methods: Between August 2009 and August 2017, 32 patients (mean age, 58.6 years) with malignant MCA infarction underwent decompressive hemicraniectomy in a regional hospital in Hong Kong. The outcome measures were mortality and the modified Rankin scale (mRS).
Results: The mortality rate was 38.7% at day 90 and day 180. About 64.5% and 58.1% of patients had unfavourable outcome (defined as mRS of >4) at day 90 and day 180, respectively. Involvement of more than one vascular territory was associated with unfavourable functional outcome at day 90 (P=0.028) and day 180 (P=0.010). Signs of herniation were associated with poorer functional outcome at day 180 (P=0.036). Neurological outcome was not associated with age, timing of surgery, or laterality of stroke.
Conclusion: About 38.7% of patients with malignant MCA infarction died after undergoing decompressive hemicraniectomy. Fewer than half of patients survived with favourable outcome. Involvement of a single vascular territory and the absence of signs of herniation were associated with favourable outcome.

DH 2

Evaluation of non-motor symptoms of Parkinson's disease patients in a Chinese population in Hong Kong

Vivianne CO Luk
Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

Background and aim: Non-motor symptoms (NMS) are prevalent in patients with Parkinson's disease and have a significant impact on quality of life, but NMS are often unrecognised by clinicians. The NMS Questionnaire (NMSQuest) is a self-administered screening tool for early detection of these symptoms. However, a Hong Kong Chinese version for local population is lacking. This study aimed to validate a Hong Kong Chinese version of the NMSQuest (HK-NMSQuest) in local patients with Parkinson's disease. The NMS profiles of another cohort of patients with Parkinson's disease were then analysed using the HK-NMSQuest.

Patients and methods: This study involved two parts. In the validation study, 78 patients with Parkinson's disease were recruited from Queen Elizabeth Hospital. They completed the HK-NMSQuest and then underwent clinical evaluation of NMS (gold standard). Sensitivity, specificity, positive predictive value, and negative predictive value in relation to the gold standard were estimated. Internal consistency was analysed. In the prevalence study, another cohort of 59 patients with Parkinson's disease was enrolled. They completed the validated HK-NMSQuest. Their NMS profiles including symptom prevalence were examined, and correlations with other parameters (patient demographics, disease duration, motor severity) were drawn. Regression analysis was performed to build a prediction model of NMS total score.

Results: In the validation study, the mean patient age was 67.0 (standard deviation [SD], 8.3) years; 56% were male; and the median disease duration was 8 (interquartile range [IQR], 6) years. Based on the gold standard, the prevalence of NMS ranged from 22.7% (orthostatic hypotension) to 90.5% (nocturia). Among the NMS, sensitivity was high for urgency (87.2%), nocturia (86.6%), and drooling (75.9%), whereas sensitivity was low for excessive daytime sleepiness (29.4%) and orthostatic hypotension (41.2%). The average sensitivity was 65.4%. Specificity was high for NMS, with an overall of 84.7%. Internal consistency (Cronbach's α) was highest in the attention/memory domain at 0.78. The mean Cronbach's α was 0.60. In the prevalence study, the mean patient age was 64.2 (SD, 9.2) years; 59.3% were male; and the median disease duration was 9 (IQR, 9) years. The mean age at onset was 54.5 (SD, 10.4) years, and Hoehn and Yahr stages ranged from 0 to 5, with a median of 2 (IQR, 2). The median NMSQuest score was 10; all patients reported to have at least one NMS. The most prevalent NMS domain was 'urinary symptoms' including nocturia (76.3%) and urgency (67.8%), whereas bowel incontinence (8.5%) and delusions (10.2%) ranked the lowest. The NMS total score was associated with education level (P=0.009), levodopa equivalent daily dose (r_s=0.476, P<0.001), and Hong Kong version Montreal Cognitive Assessment (HK-MoCA) score (r_s= −0.385, P=0.004). It was, however, not associated with patient age, Hoehn and Yahr stage, or disease duration. Multiple linear regression model showed that the Unified Parkinson's Disease Rating Scale (UPDRS) Part 2 (P<0.001) and Part 3 (P=0.004), and HK-MoCA (P=0.022) scores were independent predictors of NMS total score.

Conclusion: HK-NMSQuest was shown to be a reliable and valid tool for screening NMS in local population with Parkinson's disease. NMS are prevalent in patients with Parkinson's disease. The NMS burden was not related to age, disease duration, or Hoehn and Yahr staging, but was predictable by UPDRS and HK-MoCA. Early detection and management of NMS is important in the holistic care of patients with Parkinson's disease.

Magnetic resonance imaging volumetrics in parkinsonian syndromes

DH 3

Karen Ma
Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong SAR

Background: Advancement in magnetic resonance imaging (MRI) post-processing allows automatic and rapid quantification of regional brain volumes. This study aimed to explore the ability of such method in differentiating (1) different parkinsonian syndromes and (2) parkinsonian syndromes from normal controls.
Methods: A total of 36 patients with various parkinsonian syndromes: idiopathic Parkinson's disease (IPD) [n=10], multiple system atrophy (MSA) [n=18], and progressive supranuclear palsy (PSP) [n=8], as well as 36 controls were recruited retrospectively. 100% and 78% of the patients underwent MRI and fluorodeoxyglucose positron emission tomography, respectively, whereas all controls underwent MRI of the brain. The volume of the region of interests (ROI) on MRI of the brain was measured by an automated software (Accubrain). Differences in volume of each ROI among patients with IPD, MSA or PSP, and controls were analysed. The area under the receiver operating characteristic curve (AUC) was used to evaluate the diagnostic ability and to select the cut-off value of individual ROI with maximal sensitivity and specificity.
Results: The ratio of volume of globus pallidus to total intracranial volume (ICV) was larger in patients with IPD than in those with MSA (P=0.018) or PSP (P=0.018). The ratio of 0.189% had sensitivity of 70% and specificity of 67.4% to differentiate IPD from atypical parkinsonism, with AUC being 0.771. The ratio of caudate volume to ICV was smaller in patients with parkinsonian syndromes than controls (P<0.001). The ratio of 0.411% had sensitivity of 80.6% and specificity of 72.2% to differentiate parkinsonian syndromes from controls, with AUC being 0.829.
Conclusion: The diagnostic ability of the ratio of volume of globus pallidus to ICV was modest in differentiating IPD from atypical parkinsonism, whereas that of the ratio of caudate volume to ICV was good in differentiating parkinsonian syndromes from normal controls.

DH 4

Outcome of stroke in patients with systemic lupus erythematosus: a nested case-control study

Lap Kiu Tsoi
Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong SAR

Objectives: Stroke in patients with systemic lupus erythematosus (SLE) may cause severe disability. Outcomes of stroke in Chinese patients with SLE are unclear. This study aimed to compare the outcomes of stroke in patients with SLE and matched patients without SLE.

Methods: This was a case-control study. Patients who fulfilled ≥4 criteria of American College of Rheumatology for SLE and had a history of stroke were identified from a local SLE database. The outcomes of stroke in these patients were evaluated retrospectively and compared with a group of randomly selected age- and sex-matched patients without SLE (in a ratio of 1:3) admitted to our stroke unit within the same period.

Results: A total of 40 stroke patients with SLE (age, 53.7±11.5 years; 88% women) with stroke were identified (with the stroke prevalence of 0.39/100 patient-years) and compared with 120 matched stroke patients without SLE (age, 52.8±14.8 years; 87.5% women). The prevalence of atherosclerotic risk factors was similar in both groups, except that a higher proportion of patients with SLE had an atherogenic index of plasma of >0.21 indicating high atherosclerotic risk (P=0.002). Among patients with SLE, the median time to stroke since diagnosis of SLE was 30 months. Ischaemic strokes were more common in patients with SLE than those without (90% vs 63%, P=0.001). Among patients with ischaemic stroke, patients with SLE had more extensive infarction than controls on brain scan (69.4% vs 28.0%, P<0.002). The mean 90-day modified Rankin Scale (mRS) score was higher in patients with SLE compared with controls (1.7±2.0 vs 0.9±1.4, P=0.004). The mRS score distribution of both groups also differed significantly (P=0.003). Compared with controls, more patients with SLE were functionally dependent (mRS score of 3–6) at 90 days post-stroke (32.5% vs 8.3%, P<0.001). Logistic regression showed that SLE was an independent risk factor for poor stroke outcome after adjusting for age, sex, history of stroke, various atherosclerotic risk factors, and the type (ischaemic vs haemorrhagic) of stroke (odds ratio [OR]=10.20, 95% confidence interval [CI]=2.7–39.0, P=0.001). Subgroup analysis of patients with ischaemic stroke showed that SLE was associated with poorer functional outcome after adjusting for the same confounders and the extent of stroke (OR=44.7, 95% CI=2.9–690.9, P=0.006). Logistic regression analysis indicated that high SLE disease activity during stroke was an independent risk factor for poorer outcome (OR=19.3, 95% CI=1.4–266.1, P=0.027). The 30-day stroke mortality was comparable between patients with and without SLE (7.5% vs 2.5%, P=0.166). However, patients with SLE had a higher rate of post-stroke epilepsy than controls (22.5% vs 3.3%, P=0.001). During a mean follow-up time of 7.5±5.2 years, more recurrent stroke (ischaemic or haemorrhagic) developed in patients with SLE than in those without (40.5% vs 14.3%, P=0.001), and among patients with stroke, those without SLE had a greater survival rate than those with SLE (84.9% vs 45.2%, P<0.001).

Conclusions: Ischaemic strokes were more likely to recur in patients with SLE and in whom the infarct size was more extensive than matched controls. The functional outcome after stroke was poorer in patients with SLE. The risks of stroke recurrence, post-stroke epilepsy, and all-cause mortality were significantly higher in patients with SLE than those without.

DH 5

High-resolution sonography in the diagnosis of carpal tunnel syndrome in local Chinese population

June HM Wong
Department of Medicine and Geriatrics, Caritas Medical Centre, Hong Kong SAR

Objective: This study aimed to determine the usefulness of high-resolution sonography in the diagnosis of carpal tunnel syndrome (CTS) in patients with clinical suspicion.
Materials and methods: This prospective study recruited 58 healthy volunteers and 30 patients referred to the electrodiagnostic unit of a regional hospital in Hong Kong for CTS between January and October 2017. Within 2 weeks of the nerve conduction study, 56 wrists from the patient group and 111 wrists from the control group were evaluated by high-resolution sonography; the cross-sectional area (CSA) of the median nerve was measured at two levels: distal wrist crease (CSAc) and proximal one-third of the pronator quadratus muscle of the forearm (CSAp). Sensitivity, specificity, and accuracy of CSA in diagnosing CTS were determined, with clinical evaluation as the reference standard.
Results: The CSAc was enlarged in patients with CTS compared with controls (13.5 mm^2 vs 8.7 mm^2, P<0.001). Using clinical diagnosis as the reference standard, the area under the receiver operating characteristic curve of CSAc, the difference in CSAc and CSAp, and the ratio between CSA at the wrist and forearm were 0.931, 0.931, and 0.893, respectively (P<0.001). The CSAc was the best parameter of high-resolution sonography for diagnosing CTS, with sensitivity of 82.1%, specificity of 91.9%, and accuracy of 88.6% when the cutoff was set at 11 mm^2.
Conclusion: High-resolution sonography is a useful, non-invasive tool for diagnosing CTS and is a valuable complementary test to nerve conduction study.

Breakthrough treatment in embolic stroke of undetermined source

S 1

Lawrence KS Wong
Division of Neurology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR

Cryptogenic stroke, a subtype of ischaemic stroke under the Trial of ORG 10172 in Acute Stroke Treatment classification, has no generally accepted definition and is not defined by minimum diagnostic criteria. Therefore, this may include patients with incomplete diagnostic stroke workup and does not represent a clearly defined patient group that can be investigated in clinical trials. Embolic stroke of undetermined source (ESUS) is an embolic stroke for which no probable cause could be identified after standard diagnostic evaluations that exclude possible explanations such as small artery disease, atherosclerosis in arteries that supply the area of ischaemia, and atrial fibrillation. ESUS accounts for about one in six ischaemic strokes and has a recurrence rate of 5% per year and therefore is implicated in secondary stroke prevention therapy. Oral anticoagulation has been the standard of care for cardioembolic stroke. Clinical trials have been commenced to investigate whether oral anticoagulation is more effective than antiplatelets in preventing recurrence of ESUS. This study provides an overview on the current developments of ESUS treatment and how these developments may impact the current clinical practice.

Answer the unanswered in secondary stroke prevention in atrial fibrillation population

S 2

Peter Alan Barber
Neurological Foundation of New Zealand

Oral anticoagulation has been established as the standard of care in patients with atrial fibrillation. Patients with atrial fibrillation are at increased risk of stroke, particularly if they have had a prior episode of ischaemic stroke or transient ischaemic attack. Twice-daily treatment with 110 mg or 150 mg dabigatran, an oral direct thrombin inhibitor, has demonstrated favourable safety and efficacy profile, compared with warfarin in the Randomized Evaluation of Long-term Anticoagulation Therapy (RE-LY) trial. This presentation provides an overview on the effects of dabigatran in the subgroup of patients with previous strokes or transient ischaemic attacks in the RE-LY trial, and shares practical experiences in anticoagulating patients for secondary stroke prevention in New Zealand. The presentation also describes how the availability of idarucizumab, the specific reversal agent for dabigatran, optimises therapeutic outcomes in patients with ischaemic strokes on anticoagulation complicated by intracranial haemorrhage.

Clinical diagnosis and management of hereditary myopathies in teenage and adulthood

S 3

Zohar Argov
Department of Neurology, Hebrew University-Hadassah Medical School, Jerusalem, Israel

Even in this modern age of genetic testing by targeted or whole genome sequencing, clinical judgment remains important, because (1) whole genome sequencing is not widely available and targeted sequencing in a typical or clinically recognised syndrome may suffice for mutation analysis; (2) whole genome sequencing may show many changes that are not relevant to patient diagnosis; and (3) recognition of unusual clinical presentation may help reveal newly identified rare neuromuscular disorders, especially when a similar phenotype has been described elsewhere. The main symptoms and signs associated with hereditary myopathies are discussed. These may have implications for physical therapy and corrective surgery. Therapy of hereditary myopathies has become a leading topic in the neuromuscular field. Pharmacotherapy, aimed at metabolic supplementation or fibrosis prevention, has also been reported. However, genetic therapy is at the front now because of its potentials and high costs. Methods like RNA manipulation (exon skipping and readthrough therapy), viral mediated gene delivery, and cell therapy are reviewed.

Treatment of myasthenia gravis: from basics to advanced

S 4

Zohar Argov
Department of Neurology, Hebrew University-Hadassah Medical School, Jerusalem, Israel

Myasthenia gravis (MG) usually responds well to therapy. Since establishing the autoimmune nature of the disease, the mortality has decreased from 30% to 3%. About 80% of patients can achieve remission (full or with minimal symptoms) within several months. However, this success is not based on strong evidence-based medical grounds. In the past 45 years, fewer than 30 controlled studies have been reported. There is no consensus even on the classical modes of treatment. This presentation critically reviews the objective evidence for the impact of various therapies on the clinical picture of acquired MG. Typical case presentations are used to demonstrate the problems. The topics to be presented are: (1) A paradigm for the initial (basic) therapy stage; (2) Thymectomy: when to do it, especially after the recent completion of a long-term study; (3) Treatment of ocular MG; (4) Steroids in MG: is there an agreed protocol? (5) Which cytotoxic drugs should one use for steroid sparing? (6) Intravenous immunoglobulin treatment and plasmapheresis for MG; (7) Recognition and management of myasthenic crisis; (8) Advanced immunotherapy in myasthenia; (9) Anti–muscle-specific tyrosine kinase myasthenia: what is different in the treatment? (10) The pregnant myasthenic woman; and (11) Drug-aggravated myasthenia.

Treatment of highly active relapsing-remitting multiple sclerosis

S 5

Volker Limmroth
Department of Neurology, Cologne City Hospitals, University of Cologne, Germany

Multiple sclerosis is a chronic inflammatory disease, with relapsing-remitting multiple sclerosis being the most frequent type. Inflammation and demyelination are major pathologies leading to sustained disability via primary or secondary axonal damage and neurodegeneration. Recent studies stress the importance of early induction of highly effective anti-inflammatory therapy to prevent relapses, progression of disability, and magnetic resonance imaging activity including brain atrophy, aiming to achieve 'no evidence of disease activity'. Among immunomodulatory drugs approved within the last decade, natalizumab, alemtuzumab, and fingolimod are proved to be highly efficacious for treating relapsing-remitting multiple sclerosis with high disease activity. Nevertheless, strict pharmacovigilance is mandatory in view of potentially severe side effects, and switching to other medications may be necessary.

Management of paediatric multiple sclerosis: from adolescence to adulthood

S 6

Tanuja Chitnis
Department of Neurology, Harvard Medical School, USA

Paediatric multiple sclerosis (MS) is a highly inflammatory form of MS that usually occurs in early adolescence. Children and adolescents with MS can experience frequent relapses, cognitive deficits, and neurological decline. Disease-modifying treatments that suppress or modulate the autoimmune response have been reported, leading to the first FDA-approved therapy. This presentation reviews the current management of paediatric MS including disease-modifying and symptomatic therapies and the role of diet and lifestyle modifications. Transitional care from paediatric to adult stage is also discussed.

A new DAWN in the treatment of acute ischaemic stroke

S 7

Tudor Jovin
UPMC Stroke Institute; UPMC Centre for Neuroendovascular therapy; University of Pittsburgh School of Medicine, PA, USA

The advent of DAWN (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo) and DEFUSE-3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke) has marked a pivotal landmark amongst the newer generation of randomised clinical trials of endovascular therapy (EVT). These two latest trials have demonstrated that EVT imparts significant benefit to patients with large vessel occlusion of the anterior circulation and salvageable ischaemic penumbra at 6 to 24 h after stroke onset, similarly to patients treated before 6 h. In this presentation, the cumulative evidence from newer generation EVT trials is reviewed, along with the results of of an individual level meta-analyisis. The pathophysiological mechanisms leading to therapeutic approaches that have led to the current standard of care in stroke management are discussed. In addition, future directions for continued improvement and more widespread applicability of endovascular thrombectomy are highlighted.

Residual stenosis post-thrombectomy: an emerging challenge

S 8

Zhongrong Miao
Department of Interventional Neuroradiology, Beijing Tiantan Hospital, Capital Medical University, China National Clinical Research Center for Neurological Diseases, Center of Stroke, Beijing Institute for Brain Disorders, Beijing, China

Background and purpose: To investigate the safety and efficacy of mechanical thrombectomy plus rescue therapy for patients with intracranial large artery occlusion and underlying atherosclerosis.
Methods: Patients enrolled in the intervention group of the Endovascular Therapy for Acute Ischemic Stroke Trial were analysed. For underlying intracranial atherosclerosis identified during the stent retrieval procedure, rescue treatment was required for those with (1) a degree of >70%, (2) any degree with blood flow impairment, or (3) evidence of re-occlusion. Outcomes were compared between patients with intracranial large artery occlusion and underlying atherosclerosis and the embolic group. Multivariate logistic regression was performed to determine independent predictors of functional independence at 90 days.
Results: Of 140 patients included in the analysis, 47 (34%) were identified to have underlying intracranial atherosclerosis; 30 (64%) of them were eligible for rescue treatment; and 27 (90%) of them actually underwent rescue treatment. Patients with intracranial large artery occlusion and underlying atherosclerosis and the embolic group were comparable in terms of recanalisation rate (95.7% vs 96.8%, P=0.757) and functional independence at 90 days (63.8% vs 51.6%, P=0.169), as well as symptomatic haemorrhage (4.3% vs 4.3%, P=1.000) and death (12.8% vs 12.9%, P=0.982). Functional independence at 90 days was independently associated with National Institute of Health Stroke Score at presentation (odds ratio [OR]=0.865, 95% confidence interval [CI]=0.795–0.941, P=0.001) and modified Thrombolysis in Cerebral Infarction after the procedure (OR=2.864, 95% CI=1.018–8.061, P=0.046).
Conclusions: Mechanical thrombectomy is safe in patients with intracranial large artery occlusion and underlying atherosclerosis. The rescue treatment can achieve favourable outcomes in such patients.

Immune reconstitution therapies in multiple sclerosis: the impact on treatment decision

S 9

Anneke van der Walt
Multiple Sclerosis and Neuroimmunology Service, Department of Neurology, Monash University, Australia

The therapeutic approach for relapsing-remitting multiple sclerosis is evolving. The number of disease-modifying therapies has increased, with 13 drugs currently available to treat relapsing-remitting multiple sclerosis. These treatments are administered either continuously (ie, maintenance treatment) or intermittently (ie, immune reconstitution therapies). Health care professionals are faced with dilemma on how to personalise initial therapy and select subsequent therapies. This presentation focuses on factors associated with risk-benefit assessment in immune reconstitution therapies, including the efficacy of the disease-modifying therapies to reduce disease activity, the short- and long-term safety and immunologic profiles, the criteria for switching treatment, and the risk tolerance of each patient.

Advances in neuroimaging in central nervous system infection/inflammation

S 10

Nafi Aygun
Department of Radiology, Johns Hopkins University School of Medicine, USA

To review variable imaging appearances of neuroinflammatory disorders, to discuss the role of diffusion-weighted imaging in pyogenic and non-pyogenic abscesses, and to discuss magnetic resonance imaging features of autoimmune encephalitides.

Central nervous system infection in immunocompromised patients

S 11

Owen Tsang
Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong SAR; Hospital Authority Infectious Disease Centre, Hong Kong SAR

Infections of the central nervous system (CNS) are uncommon in immunosuppressed hosts. The overall mortality remains high despite advances in diagnostic and therapeutic technology. The type of pathogens and the severity of infections are highly related to the type of immunodeficiency and the degree of immunosuppression. Acquired immunodeficiency can be caused by impairment of (1) cellular immunity (eg, HIV infection, use of immunosuppressants for solid organ transplantations), (2) humoral immunity (eg, anti-B cell or anti-cytokine therapies for rheumatic diseases), or (3) innate immunity (eg, splenectomy). CNS infections in immunocompromised hosts can present with meningitis, meningoencephalitis, cerebritis, or brain abscesses.

In addition to common organisms that cause CNS infections, the following pathogens are also implicated: (1) bacteria: Nocardia, Listeria; (2) mycobacteria: *M tuberculosis* or non-tuberculous mycobacteria; (3) fungi: Aspergillus, Candida, Cryptococcus neoformans; (4) viruses: cytomegalovirus, Epstein-Barr virus, herpes viruses, human herpesvirus 6, John Cunningham virus; and (5) parasites: toxoplasmosis. Bacterial, viral, and fungal CNS infections commonly occur in neutropenic patients. Defects in function of T cells or macrophages predispose to cerebral toxoplasmosis and cryptococcal meningitis.

Early diagnosis is essential. However, making an accurate diagnosis based on clinical signs and symptoms can be difficult in immunocompromised patients, because of the subtle presentation and rapid progression. Any suspicion of CNS infections should prompt diagnostic procedures that encompass neuroimaging, cerebrospinal fluid (CSF) investigation, and, in some cases, brain biopsy. Molecular study of the CSF samples confers good sensitivity and specificity for a definitive diagnosis. Magnetic resonance imaging of the brain is more sensitive than computed tomography for diagnosing most CNS infections. Nonetheless, contrast computed tomography remains a good option when magnetic resonance imaging cannot be performed. Positron emission tomography can help differentiate infectious from non-infectious CNS lesions in selected patients.

Early empirical treatment is imperative because of the aggressive nature of infections. Tapering immunosuppression in solid organ transplant recipients should be considered in addition to antimicrobials, especially in case of severe bacterial or fungal CNS infections. Early anti-retroviral therapy is important for HIV-associated CNS infections. Many opportunistic CNS infections can be prevented with appropriate chemoprophylaxis and adequate CD4 recovery (CD4 count of >200 cells/mL). Vaccinations and antimicrobial prophylaxis may be considered to lower the risk of infections.

Diagnostic and therapeutic odyssey of epilepsy in the era of precision medicine

S 12

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Epilepsy remains uncontrolled with medications in one-third of patients, a ratio that has not changed despite the availability of more than 15 new antiepileptic drugs in the past 20 years. The advent of precision medicine enables personalised care in epilepsy, with therapeutics not only targeted molecularly or regionally to the specific epileptogenesis, but also tailored to the individual's genetic and other personal characteristics. This presentation discusses biomarkers, treatment stratification, and potential caveats in the progress towards precision medicine in epilepsy.

Inflammation and epilepsy

S 13

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The aetiology of epilepsy varies among different age-groups and is not well understood. Inflammation caused by infection is an important aetiology. In addition, inflammation without infection (ie, autoimmune process) has been incorporated in one of the diagnostic categories in the International League Against Epilepsy 2017 classification of seizures.

In a study of acute anti–NMDA receptor antibody encephalitis in 2007, acute non-herpetic limbic encephalitis was reported to be caused by autoimmune inflammation and mainly in young women. Afterwards, several antibodies directed against cell membrane antigens such as anti-VGKC complex antibody, anti-LGI1 antibody, anti-AMPA antibody, and anti-GABA antibody were reported to be associated with several types of focal encephalitides and autoimmune epilepsy.

Recent clinical questions and topics about inflammation and epilepsy include:

(1) Temporal lobe epilepsy (TLE) with amygdala enlargement (AE) may represent a subtype of mild autoimmune epilepsy. Initially AE was regarded as MRI-negative TLE and of epileptic focus. It accounts for 4% of TLE cases, and seizures are well controlled by drugs. The inflammatory process may be self-limiting because AE gradually disappears in many patients, with activated T-cell markers.
(2) Subacute onset of focal reflex myoclonus often suggests an underlying autoimmune disease.
(3) Chronic focal epilepsy associated with brain tumour may provoke an autoimmune process that generates multiple ictal foci, and resection of the primary tumour may result in seizure freedom.
(4) A diagnostic algorithm for autoimmune epilepsy is needed.

As the responsible antibodies of autoimmune epilepsy remain to be elucidated and promising biomarkers are not available, a diagnostic algorithm for clinical use is useful. A validation study is needed to further improve the diagnostic protocol.

FP 1

Antiplatelet treatment after transient ischaemic attack and ischaemic stroke in patients with cerebral microbleeds in two large cohorts and an updated systematic review

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Background: In patients with transient ischaemic attacks (TIA)/ischaemic strokes, microbleed-burden predicts the risk of intracerebral haemorrhage (ICH) and ischaemic stroke, but implications for antiplatelet treatment are uncertain. Previous cohort studies have had insufficient follow-up to assess the time-course of risks, have not stratified risks by anti-thrombotic use, and have not reported extracranial bleeds or functional outcome of ICH versus ischaemic stroke.

Methods: In two independent prospective cohorts with TIA/ischaemic stroke (Oxford Vascular Study comprising mainly Caucasians and University of Hong Kong study comprising mainly Chinese), antiplatelet treatment was started routinely irrespective of microbleed-burden. Risks, time-course and outcome of ICH, risk of extracranial bleeds, and recurrent ischaemic events were determined and stratified by microbleed-burden (0 vs 1, 2–4, and ≥5), adjusting for age, sex, and vascular risk factors.

Results: Microbleeds were more frequent in the Chinese than Caucasian cohort (450/1003 vs 158/1080, P<0.0001), but risk associations were similar during 7433 patient-years of follow-up. Among 1811 patients on antiplatelets, the risk of major extracranial bleeds was unrelated to microbleed-burden (P_{trend}=0.87), but was strongly related to the 5-year risk of ICH (P_{trend}<0.0001), with 11/15 (73%) of ICH in 140/1811 (7.7%) patients with ≥5 microbleeds. In addition, the risk of ischaemic stroke increased with microbleed-burden as well (P_{trend}=0.013), such that the risk of ischaemic stroke and coronary events exceeded that of ICH and major extracranial bleeds during the first year, even among patients with ≥5 microbleeds (11.6% vs 3.9%). However, this ratio changed over time, with the risk of haemorrhage (11.2%) approaching that of ischaemic events (12.0%) after one year. The association between microbleed-burden and the risk of ischaemic stroke was due mainly to non-disabling events (P_{trend}=0.007), whereas the association between microbleed-burden and the risk of ICH (P_{trend}<0.0001) was accounted for by disabling/fatal events (≥5 microbleeds: 82% disabling/fatal ICH vs 40% ischaemic stroke, P=0.035).

Conclusion: In Caucasian and Chinese patients with ≥5 microbleeds, withholding antiplatelets during the first year after TIA/ischaemic stroke may be inappropriate. However, the risk of ICH may outweigh any benefit thereafter.

FP 2

A cross-sectional survey of patients with familial amyloid polyneuropathy in Hong Kong

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Background: Familial amyloid polyneuropathy (FAP) is a rare autosomal dominant disease caused by mutation in the gene-encoding transthyretin. Progressive accumulation of amyloid fibrin from transthyretin misfolding leads to peripheral polyneuropathy, autonomic neuropathy, and restrictive cardiomyopathy. Previously, there was no effective treatment for FAP except for liver transplantation. The median survival of untreated patients is 10 to 15 years after symptom onset. Since 2011, when transthyretin stabiliser for FAP and novel molecular therapeutics became available, FAP has been treatable. Local epidemiological data on FAP is required to plan for future funding and management of this disease.
Methods: We conducted a cross-sectional survey on genetically confirmed symptomatic patients with FAP and pre-symptomatic pathological transthyretin mutation carriers identified through cascade screening. The genetic analysis was performed by the genetic laboratory in Queen Mary Hospital and Princess Margaret Hospital. Since 2015, Princess Margaret Hospital has received FAP patients referred from hospitals in other clusters in order to provide a focused and coordinated care.
Results: There were 22 Chinese patients with FAP. Their median age was 49.5 (range, 21–74) years. Of them, 20 were being followed up in Princess Margaret Hospital with FAP stage I (n=7), II (n=4), III (n=1), or 0 (pre-symptomatic) [n=8]. Genetic analysis identified six different pathological mutations: Val50Ala, Gly87Glu, Thr79Lys, Ala117Ser, Val50Met, and Val142Ala. Ala117Ser appeared to be a common mutation in local Chinese and was found in five unrelated families.
Conclusion: The local epidemiological data of FAP facilitates the understanding of the heterogeneity and management of FAP in Hong Kong.

FP 3

Risk of warfarin-associated intracerebral haemorrhage in Chinese atrial fibrillation patients with cerebral microbleeds: a prospective multicentre study

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Background: The risk of intracerebral haemorrhage (ICH) is the main factor affecting anticoagulation decision in atrial fibrillation (AF). The use of magnetic resonance imaging to detect cerebral microbleeds (CMBs), which predicts future ICH, may help guide treatment decision. We aimed to evaluate the risk of warfarin-associated ICH in Chinese AF patients with CMBs, who have higher risk of ICH than Caucasians.
Methods: In this prospective observational study, Chinese AF patients who required anticoagulation with warfarin were recruited from six hospitals in Hong Kong. 3T magnetic resonance imaging of the brain was performed to detect CMBs. Patients were followed up for 2 years. The primary outcome was clinical ICH. Secondary outcomes were recurrent ischaemic stroke, systemic embolism, and mortality of all causes.
Results: A total of 290 patients were recruited; 53 were excluded by pre-defined criteria and 237 were included in final analysis. CMBs were observed in 84 (35.4%) patients, with 11 of them had ≥5 CMBs. The mean follow-up period was 22.4±10.3 months. Compared with patients without CMBs, patients with CMBs had a trend towards higher rates of ICH (3.6% vs 0.7%, P=0.129) and ischaemic stroke (8.3% vs 3.3%, P=0.121) at 2-year follow-up. The risk of ICH was higher in patients with CMBs than in Caucasians in the CROMIS-2 study (18.5 vs 9.8 per 1000 patient-years). For patients with ≥5 CMBs, the rate of ICH was higher than that of ischaemic stroke, but the reverse was observed for patients with 0–4 CMBs. Furthermore, CMBs count (C-index=0.82) was more sensitive than HAS-BLED (C-index=0.55) and CHA2DS2-VASc scores (C-index=0.63) in predicting ICH.
Conclusions: In Chinese AF patients on warfarin, the risk of ICH was non-significantly higher among patients with CMBs. Further studies with larger sample size through international collaboration are needed to determine the risk-to-benefit ratio of oral anticoagulation in AF patients of different ethnic origins.

Intravenous thrombolysis after reversal of dabigatran's effect by idarucizumab: a case series

P 1

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Background: Intravenous thrombolysis is considered a contraindication in patients with acute ischaemic strokes on therapeutic dose of anticoagulation. With the availability of idarucizumab, patients on dabigatran can receive intravenous thrombolysis after reversal of the dabigatran's effect by idarucizumab. This study aims to investigate the safety and efficacy of this treatment approach in our hospital.
Methods: Idarucizumab has become available in our hospital since December 2016. Between December 2016 and July 2018, five patients (six cases) with ischaemic stroke on dabigatran received intravenous thrombolysis after idarucizumab was given.
Results: The median patient age was 71 years. The median initial National Institutes of Health Stroke Scale (NIHSS) score was 23 (range, 8–42). Five cases received intravenous thrombolysis alone and one received intravenous thrombolysis followed by mechanical thrombectomy. In four patients, the thrombin time was checked before and 5 minutes after idarucizumab was given; all had baseline thrombin time prolonged (range, 58.2 to >120 s), which reverted to normal (median, 18.8 s) after idarucizumab was given. Five cases had baseline activated partial thromboplastin time checked; four of them were prolonged. Five cases had major initial improvement (8-point improvement in the NIHSS score at 24 hours) and one patient was static. At follow-up, there was one minor asymptomatic haemorrhagic transformation on computed tomography of the brain. There were no other bleeding complications. One patient later developed cerebral oedema requiring craniectomy. None had thrombotic complications. On discharge, four cases had favourable outcome (with NIHSS score of ≤4 and modified Rankin score of ≤3). Two cases required assistance in daily living.
Conclusion: Intravenous thrombolysis in patients on dabigatran after reversal by idarucizumab is safe and feasible.

Sequential visual loss in a patient with biopsy-confirmed hypertrophic pachymeningitis

P 2

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Hypertrophic pachymeningitis is a rare condition characterised by chronic inflammation and thickening of the dura mater. Its diagnosis remains challenging. We report an 86-year-old Chinese man who had biopsy-confirmed hypertrophic pachymeningitis with possible underlying IgG4-related disease. The patient presented with visual loss of fluctuating severity and numbness of his left forehead. He had a history of asthma, hypertension, and chronic renal failure associated with myeloperoxidase-antineutrophil cytoplasmic antibodies–associated crescentic glomerulonephritis. On examination, he was fully conscious and afebrile. There was loss of light touch sensation over his left forehead. Visual acuity of his right and left eye fluctuated from light perception to 0.2 and from 0.05 to 0.3, respectively. The rest of the neurological examination was unremarkable. Laboratory investigation revealed elevated erythrocyte sedimentation rate and C-reactive protein. He had mild leukocytosis of 11.4 $\times 10^9$/L. Anti-nuclear antibody and anti-neutrophil cytoplasmic antibody titres were normal. Cerebrospinal fluid analysis revealed lymphocytic pleocytosis, elevated protein of 1.16 g/L, but bacterial, mycobacterial, viral, and fungal cultures were negative. Non-contrast magnetic resonance imaging of the brain showed a 0.3-mm dural thickening surrounding the left cerebral hemisphere relating to subdural haematoma, as shown on previous computed tomography. In view of the unresolved clinical condition and lack of history of trauma, biopsy of the left dural thickening was performed. Microscopic examination showed features compatible with hypertrophic pachymeningitis, but the immunostaining results were neither diagnostic nor exclusive for IgG4-related disease. Concurrent temporal artery biopsy revealed no clear evidence of giant cell arteritis. Serum IgG4 was later found to be elevated to 2.024 g/L (normal range, 0.168–1.000 g/L). A diagnosis of hypertrophic pachymeningitis with possible IgG4-related disease was made. Pulsed steroid followed by a tapering course of oral prednisolone was prescribed. The patient's left forehead sensation soon returned but the visual acuity only improved slightly and became static afterwards. Hypertrophic pachymeningitis poses a diagnostic challenge. With a lack of sensitive and specific serum biomarkers for this condition, a high index of clinical suspicion is especially important. Tissue biopsy remains the gold standard for diagnosis.

AUTHOR INDEX

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