

Economy Class Stroke and Transient Ischaemic Attack

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Bun Sheng, Ho-lun Li, Kwok-kwong Lau, Ping-tim Tsui
Princess Margaret Hospital, Hong Kong SAR

Background: Economy class stroke and transient ischaemic attacks (TIA) are cerebral thromboembolic events occurred during or shortly after long-distance aircraft travel. Typical patients described in the literature do not have conventional vascular risk factors, and a paradoxical embolisation through a patent foramen ovale (PFO) has been proposed as the primary aetiology in those patients. Being the nearest hospital to the airport, we have the privilege to see all these referrals.

Methods: A retrospective case review on patients admitted directly from the airport with ischaemic stroke or TIA from 1 January 2003 to 31 December 2006.

Results: Eleven patients (8 male and 3 female; 8 Caucasians, 2 Asians, and 1 African) were recruited, with a mean age of 57.4 (range, 38-76) years. Nine patients were intercontinental travellers (4 from Europe, 3 from North America, 1 from Africa, and 1 from Middle East), the other two patients were from Japan. Six of them had stroke (4 partial anterior circulation infarction, 1 posterior circulation infarction, and 1 lacunar stroke) and the rest had TIA (4 anterior circulation and 1 vertebrobasilar). Conventional vascular risk factors were present in only six patients. One patient developed deep vein thrombosis and pulmonary embolism shortly after admission for stroke, but the echocardiogram could not identify PFO. The patient with posterior circulation infarction died after 5 days of treatment. Among the other five stroke patients, two were transferred to private hospital within the first 2 days, one was discharged on day 6, and the remaining two patients received in-patient rehabilitation and returned to home country on day 30 and 31.

Conclusion: Economy class stroke is a heterogeneous entity. Some patients may share similar thromboembolic mechanisms to conventional ischaemic stroke, but in many cases causes are unexplained. We could not identify a single dominant aetiology in our group of patients.

Response to Drug Therapy in Patients with Epilepsy

F 2

Eric Sze-wai Yeung, Chun-ming Cheung, Tak-hong Tsoi
Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

Background: Response to drug therapy in patients with epilepsy had been studied extensively. Older population-based or hospital-based studies showed the chances of achieving remission were between 65% and 75%.

Methods: In our hospital, the source of patients can be from emergency admission, referral from primary care, paediatric unit, or other hospitals. Eligible patients were identified by the diagnosis coding of epilepsy. Those fulfilling the following criteria were entered into the cohort: (1) onset of epilepsy between 1994 and 2003; (2) patient was followed up in out-patient clinics during the whole year of 2004; and (3) for those who defaulted follow-up or died before 2004, seizure control in the last year of follow-up was assessed instead. The patients' data in hospital admission records and out-patient follow-up notes were retrieved and retrospectively reviewed for seizure control in the year 2004 or the last year of follow-up. Patients with no single seizure in the whole year of 2004 or the last year of follow-up were considered as in remission. Patients with a single seizure or more were considered as refractory irrespective of the cause, including poor drug compliance. An epileptic drug would be considered as drug failure if the patient still had seizures while taking the drug or changed to another drug because of side-effect or intolerance.

Results: The study consisted of a cohort of 298 patients, 177 male and 121 female. The mean age was 56.1 years. The percentages of remission were respectively 52.7%, 18.1%, 4.4%, 1.6%, and 1% after taking the first, second, third, fourth, and fifth drug.

Conclusion: The response to drug treatment was good in our hospital-based study. We have 77.8% of patients becoming seizure-free for at least 1 year after trying a different number of drugs.

The Usefulness of C3 Level in Differentiating Multiple Sclerosis from Systemic Lupus Erythematosus

Kwok-kwong Lau, Yuet-ping Yuen, Ho-lun Li, Bun Sheng
Princess Margaret Hospital, Hong Kong SAR

Background: To diagnose multiple sclerosis (MS), neurologists have to distinguish MS disease from other medical illnesses. Systemic lupus erythematosus (SLE) is well-known that can mimic MS in many aspects. Neurologists have to screen for markers of SLE before diagnosing MS. A low C3 level is one of the many markers that will alert neurologists of the possibility of SLE. Most, if not all, local hospital laboratories use C3 reference intervals provided by the reagent manufacturers. The aim of this study was to evaluate the C3 reference interval used in our hospital laboratory using serum samples collected from apparently healthy adults.

Methods: We screened 59 apparently healthy subjects who worked in the Princess Margaret Hospital. Their blood samples were collected as part of the "Caring Your Heart Program". None of them had a history of renal disease, vasculitis, or encephalopathy. All serum samples were frozen and analysed within 8 days after collection. C3 level in these samples were measured using Immage, Beckman Coulter. The reference interval provided by the reagent manufacturer was 0.79 to 1.52 g/L.

Results: Fifty-nine serum samples were collected from adult subjects with no evidence of SLE. The female-to-male ratio was 26:33. The ages of these subjects ranged from 23 to 64 years, and the mean age was 37 years. Among the 59 serum samples, 12 (20.3%) had C3 levels lower than the lower reference limit of 0.79 g/L. The lowest C3 level was 0.61 g/L and the patient was fully asymptomatic with no clinical evidence of vasculitis or SLE.

Conclusion: One fifth of the studied subjects had low serum C3 levels when compared to the reference interval provided by the reagent manufacturer. We need to develop our normal range for C3 level, which probably requires larger samples. While longitudinal follow-up will also help in making a diagnosis, other tests such as ANA, ANA titre, anti-dsDNA can be useful. C3 level has its limitation in screening for early SLE. While a sharp clinical alertness cannot be substituted, a normal range which suits our population will provide better screening for immunological diseases.

Prognosis of Chinese Patients with Stroke Associated with Small Vessel Disease (SSVD): a 3-year Follow-up Study

Alexander Lau, Adrian Wong, HK Ng, Larry Baum, Lawrence Wong, Vincent Mok, Wynnie Lam
Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong SAR

Background: Stroke associated with small vessel disease (SSVD) is the most commonly encountered subtype of ischaemic stroke. We aimed to study the long-term prognosis and to identify risk factors predictive of poor outcome.

Methods: Between January and June 2002, 75 (29.2%) consecutive patients admitted to the acute stroke unit of a tertiary hospital were diagnosed SSVD; stroke aetiology was established by clinical assessment, computed tomography, magnetic resonance imaging (MRI), transcranial doppler, and carotid duplex ultrasound. These patients were followed up for 36 months. Both classical and novel risk factors in the assessment of clinical outcome, including death and recurrent stroke, were identified.

Results: 14% (n=11) patients died during follow-up; 14% (n=11) patients had recurrent stroke, of which 36% (n=4) were fatal. The most common causes of death were pneumonia and recurrent stroke. These patients were usually older (79.7 vs 69.1 years, $P=0.03$) and had higher National Institutes of Health Stroke Scale (NIHSS) score on admission (6.8 vs 3.9, $P=0.0004$). On MRI, white-matter-change volume (WMC) ≥ 5.5 mL had significant predictive value of survival and recurrent stroke (HR=7.72 and 7.62 respectively, $P=0.03$). Recurrent stroke patients had worse renal function as assessed by Modified Diet for Renal Disease equation (MDRD) adapted for Chinese (66.8 vs 79.7 mL/min, $P=0.047$). Moreover, presence of microbleeds on MRI (HR=4.44, $P=0.051$) and hyperhomocysteinaemia (HR=6.96, $P=0.025$) predicted risk of recurrent stroke.

Conclusion: The 36-month prognosis of SSVD patients is favourable but not totally benign. Clinical assessment of renal function by MDRD, NIHSS, and radiological assessment of microbleeds, and WMC predict risk of recurrent stroke and mortality. A larger cohort study is required to validate these findings.

Anne Chan¹, Christine Lau², John Chan³, Jonas Yeung⁴, KL Tsang⁵, Mandy AuYeung⁶, Nelson YF Cheung³, TH Chung⁵, Vincent Mok²

¹ Prince of Wales Hospital, Hong Kong SAR

² The Chinese University of Hong Kong, Hong Kong SAR

³ Queen Elizabeth Hospital, Hong Kong SAR

⁴ Alice Ho Nethersole Hospital, Hong Kong SAR

⁵ Private practice, Hong Kong SAR

⁶ Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

Background: Although development of wearing-off phenomenon may represent disease deterioration that requires modification of medication in Parkinson's Disease (PD) patients, patients may not volunteer to inform physicians of such changes and physicians may not have time to enquire patients on its development. This pilot study aimed to validate a Chinese Version of the Wearing-off Questionnaire (WOQ) for detection of wearing-off phenomenon among Chinese PD patients.

Methods: The original English-validated WOQ-9 was designed for PD patients to complete so as to aid physicians in detecting wearing-off phenomenon in a busy clinic. The WOQ-9 was translated into Chinese. Explanations on certain terms were added into the Chinese version. Thirty-seven Chinese PD literate patients were first asked to complete the Chinese-translated WOQ-9 (CWOQ-9). All the patients were then assessed by neurologists for confirming the absence or presence of wearing-off phenomenon. Concurrent validity of CWOQ-9 was evaluated using neurologists' assessment as the gold standard by the Spearman correlation.

Results: The mean age of the 37 patients was 61 (SD, 9) years; 24% (n=9) were female. Disease duration was 6 (SD, 4) years and the mean levodopa dosage was 366 (SD, 292) mg. Twenty-four (65%) of the patients were diagnosed to have wearing-off phenomenon by the neurologist. The Spearman correlation between CWOQ-9 and neurologists' assessment was 0.37 ($P=0.022$), while kappa was 0.36 ($P=0.02$). Eleven (30%) patients appeared to have misinterpreted the questionnaire.

Conclusion: The present CWOQ-9 has only fair correlation with neurologists' assessment. Further revision of the present CWOQ-9 is needed before it can be used in clinical practice.

Deep Brain Stimulation (DBS) in Advanced Parkinson's Disease: a Local Experience

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Yuk-fai Cheung¹, Fung-ching Cheung², John Hiu-ming Chan¹, Hiu-fai Chan¹, Judy Mi-kuen Tin², Samuel Cheong-lun Leung², Patrick Chung-ki Li¹

¹ Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

² Department of Neurosurgery, Queen Elizabeth Hospital, Hong Kong SAR

Background: Deep brain stimulation (DBS) is a therapeutic option for advanced Parkinson's disease (PD) patients who suffer from medically refractory motor fluctuations and dyskinesias.

Methods: Our data from July 2000 to July 2007 were retrospectively analysed.

Results: Eighteen patients (7 men) with a mean (SD) age of 55.00 (9.33) years at the time of surgery and a mean disease duration of 11.13 (4.36) years were included. Fourteen patients were followed for more than 12 months; mean (SD) off-medication score on UPDRS part II decreased from 19.57 (7.90) before surgery to 13.55 (5.72) after surgery ($P=0.02$). UPDRS part III decreased from 33.86 (14.49) to 17.64 (7.67) [$P=0.02$]. The mean duration of off-period decreased from 1.71 (0.91) to 0.90 (0.99) [$P=0.05$]. The mean disability related to dyskinesias decreased from 1.57 (1.09) to 0.18 (0.40) [$P=0.01$]. The mean duration of dyskinesias decreased from 1.86 (1.23) to 0.73 (1.01) [$P=0.06$]. The mean dose of anti-parkinsonian medications was significantly reduced (levodopa equivalent 810.36 [410.15] to 410.05 [280.01] mg/day, $P=0.006$). Significant weight gain was noted after DBS (54.88 [8.84] to 62.91 [6.74] kg, $P=0.02$). Complications included transient delirium (3), pneumonia (1), suboptimal lead position (1), minor frontal haemorrhage near the lead entry zone and delirium (1), and apraxia of eyelid opening and lingual dystonia (1). Revision of implantable pulse generator due to device problem was required for one patient (revised during contralateral lead implantation). There was no mortality. Battery exhaustion was encountered in two patients (battery lifespan, 5 and 7 years).

Conclusion: Deep brain stimulation is a safe procedure and improves off-symptoms and motor complications in advanced PD patients.

Outcome of Patients with Concurrent Coronary and Carotid Atherosclerosis

F 7

CH Lo, PW Ng

United Christian Hospital, Hong Kong SAR

Background: Local data concerning the prevalence and outcome of patients with concurrent coronary and carotid atherosclerosis are limited. Controversy concerning management of concurrent disease remains unresolved.

Methods: This was a retrospective cohort study of patients indicated for coronary artery bypass surgery (CABG) in the United Christian Hospital (a regional hospital in Hong Kong) during the period of November 2003 to August 2005. The associated risk factors and the outcome with concurrent disease were analysed.

Results: Sixty-two patients were indicated and referred for CABG during the study period. Thirty-eight patients underwent either carotid Doppler ultrasound study or carotid angiogram preoperatively. Ten (26%) patients were found to have concurrent coronary and carotid atherosclerosis. Coronary artery bypass surgery was performed in 44 (71%) patients eventually, of which 30 (68%) underwent screening for concurrent carotid disease prior to CABG. Five (17%) patients were found to have haemodynamically significant carotid stenosis. Six patients died after CABG and the 30-day mortality was 4.5% (2/44). Two of five patients with confirmed carotid stenosis undergoing CABG survived, one of them underwent carotid stenting prior to CABG (ie 60% mortality for patients having concurrent coronary and carotid atherosclerosis underwent CABG). All the deceased patients were found to have concomitant renal impairment and left main stem disease of the coronary arteries.

Conclusion: Concurrent renal impairment and left main stem disease appeared to be associated with underlying carotid atherosclerosis and poor prognosis in patients with underlying coronary artery disease undergoing CABG. Preoperative screening for concurrent carotid atherosclerosis in this group of patients undergoing CABG is advocated.

Intravenous Tissue Plasminogen Activator (TPA) for Treatment of Acute Ischaemic Stroke—Predictive Factor for Good Outcome

Sonny FK Hon, TH Tsoi, CM Cheung, M AuYeung, CN Lee, R Li
Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

Background: Data on the use of tissue plasminogen activator (TPA) for acute ischaemic stroke in Hong Kong are limited.

Methods: We reported a 5-year retrospective review of the use of TPA treatment for acute ischaemic stroke from the data of our stroke database.

Results: Thirty-nine patients were given TPA for acute ischaemic stroke from January 2003 to September 2007—three (0.4% of all ischaemic stroke admission) in year 2003, six (0.9%) in 2004, seven (1.0%) in 2005, 13 (1.7%) in 2006, and 10 (2%, up to September) in 2007. One case was excluded for analysis as the final diagnosis was acute internal carotid artery dissection. The age ranged from 42 to 91 years, with a mean (SD) of 72.5 (11) years. Mean National Institutes of Health Stroke Scale (NIHSS) score on admission was 21.4 (SD, 7.8). Nineteen patients showed >3 points improvement in NIHSS after TPA treatment. Thirteen (34.2%) patients showed ≥ 10 points major improvement. On discharge, 39.5% had <10 points in NIHSS, and 18.4% with >20 NIHSS (excluding 9 deaths), compared with only 8.1% with <10 point NIHSS and 49.5% with >20 point NIHSS on admission. Mortality rate was 23.7%. The mean NIHSS score on admission was 26 (range, 20–36) in this group, none have improvement after TPA treatment, indicated failed treatment. No detrimental effect from TPA was observed in this group. One patient developed multiple superficial bruise over the body after TPA treatment. One patient developed symptomatic haemorrhagic transformation with headache, but there was no worsening of neurological deficit. Three patients had asymptomatic haemorrhage. Younger age (≤ 75 years) was the only factor associated with a higher chance of improvement ($P=0.01$). Improvement was noticed in 70% of younger patients compared with 27.8% in older patients. Fewer younger age patients had hypertension (40% vs 83.3%, $P<0.01$).

Conclusion: In a careful selected group of acute ischaemic stroke patients in a regional general hospital, use of intravenous TPA was safe and had encouraging result. Age was an important factor in predicting outcome of TPA treatment.

Retrospective Study of Tuberculosis Meningitis: a Hong Kong Regional Hospital Experience

R Li, CM Cheung, CN Lee, SFK Hon, M AuYeung, KL Shiu, TH Tsoi
Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

Background: Tuberculosis prevalence is increasing in Hong Kong in recent 10 years. Tuberculosis meningitis (TBM) is one of the most devastating tuberculosis infections that we need to tackle in neurology practice. Prevalence and clinical outcome are not clear locally. Therefore we investigate the prevalence, clinical presentation, treatment, and clinical outcome of TBM patients in Pamela Youde Nethersole Eastern Hospital (PYNEH) from 1994 to 2006.

Methods: All patients diagnosed with TBM from 1994 to 2006 were identified from the database of PYNEH computer system and recruited into the study. All hospital records, out-patient progress notes, and electronic records were retrieved and critically reviewed. Data on patients' demographic characteristics, clinical presentation, investigations including microbiological and radiological studies, treatment, and clinical outcomes were systematically analysed.

Results: A total 42 patients with TBM were identified. The annual incidence of TBM was 0.65/100 000. The mean age of our TBM patients was 41.9 years, with a male-to-female ratio of 52.3:47.6. The median presentation time from symptoms onset was 7.5 (range, 1-160) days. The severity on admission, by Medical Research Council classification, was: stage I 73.8%, stage II 19%, and stage III 7.1%. The most common presenting symptoms were fever (73%), confusion (58.8%), and headache (55.9%). The results of cerebrospinal fluid (CSF) analysis were: positive acid-fast bacilli smear 15.4%, positive culture 43.6%, median CSF opening pressure 23 cm H₂O, white blood cell count 176.4 /mm³, mean lymphocyte count 80%, mean protein 3.12 g, mean glucose 2.28 mmol/L. 92.9% received standard drug regimen of HRZM+/-S (H=isoniazid; R=rifampicin; Z=pyrazinamide, M=ethambutol; S=streptomycin); 85.7% were treated with systemic corticosteroid. The following complications were seen: hydrocephalus 19.5%, tuberculoma 7.3%, cerebral oedema 2.4%, arachnoiditis 9.5%, cerebral infarct 4.8%, and ventriculitis 2.4%. Mortality rate related to TBM was 16.7%. 71.4% patients had good recovery and could walk independently at the time of analysis.

Conclusion: The prevalence of TBM is stable throughout despite increasing incidence of all tuberculosis infections. Case mortality and outcomes are relatively good in our cohort of patients.

CN Lee

Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

Background: High early risk of stroke after transient ischaemic attack (TIA) was reported in several prospective population-based cohort studies. The early risk reported in these studies was associated with certain clinical factors, characteristics of TIA, vascular territory, underlying pathology, and brain imaging results. Large artery disease was found to have a higher rate of recurrent stroke or vascular mortality than patients with lacunar event. Intracranial large vessel disease has not been studied before which is important in our locality. Recently, scoring systems have been developed for predicting risk of stroke after TIA. For instance, the ABCD prognostic score in the United Kingdom and the California score in the United States are used to predict the 7-day and 90-day of stroke respectively after TIA. These scoring systems have not been validated in Chinese population.

Methods: We conducted a retrospective review from a prospectively collected database between 1 January 2004 and 31 December 2005. The 6-point ABCD score (Table) was calculated in each TIA patient based on the clinical features and other characteristics upon presentation. For every TIA patient who later developed stroke within 1 year, we selected two TIA patients without stroke in our cohort matching for sex, age, and risk factors in forming the case control in order to study the effect of underlying TIA mechanism on the risk of subsequent stroke.

Results: We found that the short-term risk of ischaemic stroke after TIA was high (10.6% at 7-day, 13.2% at 90-day, and 17.5% at 1-year.) Clinical feature of focal weakness was found to be a significant risk factor for stroke after TIA (7-day and 90-day). Isolated visual or sensory symptom was found to be low risk for stroke. There was a higher risk of stroke in patients with large vessel disease though it was not statistically significant. By using cut-off point of ≥ 4 to predict 7-day risk of stroke, the sensitivity, specificity, positive predictive value, and negative predictive value were 1.0, 0.27, 0.14, and 1.0, respectively.

Conclusions: The clinical features of TIA provided prognostic information in predicting the short-term risk of stroke. A higher risk of stroke was observed in our Chinese patients with large vessel disease. Concerning the ABCD score, it seems to have some predictive value in our group of Chinese patients in predicting 7-day risk of stroke after TIA.

Table. The 6-point ABCD score

Risk factor		Points
Age (years)	≥ 60	1
Blood pressure	Systolic >140 mm Hg and/or diastolic ≥ 90 mm Hg	1
Clinical features	Unilateral motor weakness	2
	Speech disturbance without weakness	1
	Others	0
Duration of symptoms (minutes)	≥ 60	2
	10-59	1
	<10	0

HW Leung

Department of Medicine and Therapeutic, Prince of Wales Hospital, Hong Kong SAR

Background: Semiology distinguishing mesial-frontal seizures from lateral-frontal/orbitofrontal seizures helps with presurgical evaluation of refractory epilepsy. The clinical utility of mesial-frontal semiology was evaluated and calculated.

Methods: In the first part of study, 152 patients undergoing frontal-lobe surgery (1997-2005) were further selected if seizure-localisation was achieved by analysis of resection margins (mesial-frontal/lateral-frontal/orbitofrontal), intracranial exploration and achievement of Engel-class I outcome. Eighty-four patients had their habitual seizures (167 seizures) analysed by video-encephalography (VEEG) using a semiology checklist of 47 items during the early phase (electrographic onset to 10 s) and late phase (rest of seizure episode). Localisation semiology was analysed by χ^2 test with Bonferroni correction and cluster analysis when occurrence exceeded 10% in at least one region. In the second part of the study, 253 patients undergoing non-frontal-lobe surgery (1997-2005) were further selected if seizure-localisation was achieved by the same method as above. A total of 144 patients had their habitual seizures (288 seizures) analysed by VEEG regarding the mesial-frontal semiology from the first part of the study (early phase only).

Results: The statistically significant localising semiology for mesial-frontal region in the early phase was ictal body-turning along horizontal body axis (BT1) [58.2%], crawling (58.2%), restlessness (56.4%), facial expressions of anxiety (41.8%), fear (36.4%), grimacing produced by bilateral facial contraction (34.5%), barking (30.9%), headshaking (23.6%), pelvic-raising (23.6%) and semi-turning (18.2%) [all $P < 0.00143$]. In the late phase, hyperkinetic lower-limb movement (25.5%) and recurrent utterances (16.4%) were additional statistically significant items (all $P < 0.00161$). BT1 gave a 55% positive predictive value which may increase to 86% when clustered with restlessness, anxiety, fear, and barking.

Conclusion: Ictal body-turning along horizontal body axis and semiology with physiological movement are not only prevalent semiology items of mesial-frontal lobe epilepsy but they also distinguish mesial-frontal seizures from lateral-frontal/orbitofrontal seizures.

Use of Magnetic Resonance Angiography (MRA) to Predict Long-term Outcomes of Ischaemic Stroke Patients with Concurrent Intracranial and Extracranial Stenoses

BL Man^{1,2}, YP Fu¹, YY Chan², W Lam³, CF Hui², WH Leung², KS Wong²¹ Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong SAR² Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong SAR³ Department of Diagnostic Radiology and Organ Imaging, Prince of Wales Hospital, Hong Kong SAR

Objective: To determine the long-term outcomes of ischaemic stroke patients with concurrent intracranial and extracranial atherosclerosis using magnetic resonance angiography (MRA).

Methods: A prospective cohort of patients with acute ischaemic stroke was studied with MRA of brain and carotid duplex for extracranial stenoses. All patients were followed up regularly for the development of recurrent stroke, cardiac event, or death.

Results: A total of 343 patients with acute ischaemic stroke were included, of whom 104 had concurrent intracranial and extracranial lesions. The follow-up period was up to 76 months (mean, 44.5 months). Overall, 53 (15.5%) patients died of any cause and 91 (26.5%) patients suffered a further non-fatal vascular event. The overall 5-year cumulative rates of mortality, restroke, and poor outcome were 18%, 27%, and 37%, respectively. In patients with concurrent lesions, these rates were 31%, 41%, and 51% respectively. The corresponding rates were 13%, 22%, and 31% in patients without concurrent lesions. The risks were highest in the first year after stroke. More deaths (log rank, 16.3; $P = 0.0001$), restrokes (log rank, 9.71; $P = 0.002$) and poor outcomes (log rank, 13.87; $P = 0.0001$) were found among patients with concurrent lesions. In Cox proportional-hazards regression model, the presence of concurrent vascular lesions, advanced age, smoking, hyperlipidaemia, and previous history of stroke were independent predictors of poor outcomes.

Conclusions: The long-term prognosis of ischaemic stroke patients with concurrent atherosclerosis of intracranial and extracranial vessels is poor. They are at high risks of further vascular event or death. Our findings provide important data for planning future randomised clinical trials for this high-risk group of stroke patients.

Y Soo

Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong SAR

Background: Silent cerebral microbleeds (MB) are frequently identified in stroke patients by gradient-echo T2*-weighted magnetic resonance images (MRI). Several retrospective studies suggested that MB are associated with increased risk of intracerebral haemorrhage (ICH), leukoaraiosis, and lacunar infarct. Treatment for ischaemic stroke patients with MB, therefore, becomes challenging. The aim of this study was to assess the burden of MB in ischaemic stroke patients and their influence on patients' outcome. We also evaluated the role of MB as a predictor for future ICH.

Methods: We analysed MRI images of 1016 patients admitted consecutively for acute ischaemic stroke to Acute Stroke Unit in a regional hospital between January 1999 and November 2004. Lesion load and distribution of MB, as well as white matter change, were documented. Radiological features were correlated with outcomes events (subsequent ICH, recurrent infarct and mortality) using multivariate analyses.

Results: Microbleeds were identified in 28.5% (290/1016) of patients. Presence of MB was significantly more common in patients with hypertension, prior ICH, and subsequent ICH, and they were more frequently found in the thalamus. Multivariate analysis showed that MB (HR=6.142; P=0.002; 95% CI, 1.976-19.113) and age (HR=1.082; P=0.008; 95% CI, 1.021-1.147) were the only independent predictors for subsequent ICH. White matter change was a common associated finding that combination of MB and white matter change might represent an advanced stage of microangiopathy with bleeding tendency. ROC showed that MB ≥ 8 has a sensitivity of 58.3% and specificity of 80.6% in predicting subsequent ICH.

Conclusion: In ischaemic stroke, gradient-echo T2*-weighted MRI sequence is important for risk stratification. Asymptomatic MB can be commonly found in ischaemic stroke patients and is an independent predictor for future ICH. When managing patients with MB, risk and benefit of anti-thrombotic agents should be carefully weighed. Extra cautions should be taken to minimise risk of future ICH. Nevertheless, MB should not be used alone for risk stratification. Other clinical factors, especially age, should be taken into consideration when determining risk of haemorrhage.

Diagnostic Profiles of 454 Consecutive Patients Referred for Cognitive Evaluation in Memory Clinic, and the Impact of Vascular Pathology on the Progression of Probable Alzheimer's Disease Dementia

B Sheng

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

Background: Co-existence of Alzheimer's disease (AD) and cerebral infarction (CI) is common in dementia patients. Their combination is heterogenous, and the current classifications do not provide a good conceptual framework for describing these patients. In this study we evaluated the disease pattern seen in a multidisciplinary memory clinic and examined the vascular risk factors, prevalence of cerebral ischaemic lesions, and their impact on disease progression in dementia patients. We hypothesised that those AD plus CI patients with their CI satisfying the NINDS-AIREN neuroimaging criteria for vascular dementia (VaD), which select the CIs with strong influence on cognition, progress faster.

Methods: This is a retrospective cohort study on the 454 consecutive patients presenting to the memory clinic of the Princess Margaret Hospital from 1 January 1999 to 30 June 2004. Essential clinical information including diagnosis, investigation, cognitive assessment, and progression during follow-up was registered according to the clinic protocol. We divided the study into two phases. The first phase was a cross-sectional survey on the diagnostic pattern on all 454 patients in order to give an overview on the disease spectrum in the memory clinic. The second phase assessed the impact of CI in AD patients and included only those AD patients, with or without CI, who had been followed up regularly for more than 1 year and be initially community-dwelling upon their first clinic visit. Accordingly, 130 patients were identified. We classified them with regard to the distribution and severity of CI as defined by the NINDS-AIREN neuroimaging criteria into AD-N (no CI), AD-I (CI but not fulfilling neuroimaging criteria), and AD-V (CI fulfilling neuroimaging criteria), and tested their difference in dementia progression. We defined the loss of self-independence, indicated by institution admission, or a clinical dementia rating (CDR) score of 3, as endpoints for poor outcome.

Results: Phase I—Among the 454 patients, 84.8% were diagnosed dementia and 27 had mild cognitive impairment. Reversible dementia was identified in 24 patients and normal cognition in 18. In patients with dementia, 55.8% had AD, followed by VaD (26.2%), other irreversible dementia (6.0%), dementia of Lewi bodies (5.2%), undetermined dementia (4.9%), and frontotemporal dementia (1.8%). Median duration from symptom onset to medical consultation was 2 years, 66.5% had advanced disease with initial MMSE of ≤ 17 . 85% were community-dwelling upon their first visit, and 80% of them need assistance in daily living. Phase II—130 patients were included, with a mean age of 75.8; 68.5% were women. The initial MMSE was 15.3 ± 0.4 , and the mean duration of follow-up was 30.4 months. Fifty-four patients had reached study endpoint at the time of analysis. AD-V (HR=3.1 [1.2-8.2]), use of psychotropic drugs (HR=2.7 [1.1-6.4]) and initial MMSE (HR=0.9 [0.8-1.0]) were independent predictors of poor outcome in the Cox-regression model.

Conclusions: The distribution of different types of dementia is similar to the local population survey. Patients with memory problems presented late to medical attention, resulting in a high proportion of advanced dementia. In AD, co-occurrence of CI with distribution and severity as defined in the NINDS-AIREN neuroimaging criteria for VaD is associated with fast dementia progression.

E Wong

Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong SAR

Background: Cerebral blood flow (CBF) increases after carotid revascularisation. Occasionally this increase is severe and causes cerebral hyperperfusion with adverse clinical outcome. Transcranial doppler (TCD) measurement of middle cerebral artery (MCA) flow velocity is one of the tools to evaluate cerebral hyperperfusion although its use is limited in patients with poor temporal acoustic window. This study aimed to assess the changes in flow velocities of intracranial arteries after carotid angioplasty and stenting (CAS), in particular the feasibility of using carotid siphon via orbital window as a measurement site for its ease to obtain doppler signal.

Methods: Consecutive patients with CAS done between September 2006 and April 2007 were recruited from the neurology unit of a regional hospital. Transcranial doppler was performed on these patients within 1 week before and 1 day after the procedure. The pre- and post-CAS MCA and carotid siphon peak systolic flow velocities (PSV) were compared.

Results: Twelve patients with 17 CAS (5 patients with bilateral CAS) were included. None developed cerebral hyperperfusion syndrome after CAS. Adequate temporal window ipsilateral to CAS was identified in 10 out of 17 cases. The mean PSV of MCA increased from 89.7 to 105.5 cm/s after CAS ($P=0.046$) in these 10 cases. Carotid siphon doppler signal was detected in all 17 cases. The PSV of ipsilateral carotid siphon increased from 76.4 to 92.9 cm/s ($P=0.019$). The increase in carotid siphon PSV was higher in patients with severe carotid stenosis compared to moderate stenosis (23.4 vs 6.9 cm/s, $P=0.036$). A correlating trend was apparent between the increases of MCA and carotid siphon PSV but it was not statistically significant ($r=0.573$, $P=0.084$).

Conclusion: Patients with severe carotid stenosis had larger increase in intracranial blood flow velocity after CAS and may be at a higher risk of post-CAS cerebral hyperperfusion. The use of carotid siphon as a measurement site appeared feasible. Further studies with larger sample size are required to confirm the correlation of MCA and carotid siphon PSV and to define the threshold values for cerebral hyperperfusion as measured from carotid siphon.

YF Koo

Department of Medicine, Tseung Kwan O Hospital, Hong Kong SAR

Background: Over the years, charcoal burning has almost unnoticeably become the most predominant form of suicide undertaken in Hong Kong. Apparently patients who suffered from CO poisoning were presented with variable neuropsychiatric outcomes. Proven facts also suggested that it brought about a conspicuous health problem associated with high incidence of severe mortality and morbidity. This paper pertains to a cross-sectional study on carbon monoxide (CO) poisoning survivors recruited from a regional hospital between July 2000 and July 2005. The primary aim of this study was to probe into various outcomes of this form of poisoning in terms of their neurology and psychiatry, with a bid to generate a temporal sequence of neuropsychiatric sequelae correlating to CO hypoxic insult.

Methods: Patients recovered from CO poisoning between July 2000 and July 2005 were recruited to form the sample base. These patients were invited back to the hospital for an assessment study. Their results, together with data extracted from previous relevant medical records, were analysed and studied.

Results: Nineteen survivors initially agreed to participate in this study but only 17 eventually joined. Of those participated, it was found that 90% of them suffered from mild-to-moderate degree cognitive impairment while more than 60% of them had varying degrees of depressive features. Two survivors presented with variable neurology including extrapyramidal features and Parkinsonism. Seemingly, depressive features and cognitive impairment were some common delayed manifestations. Their admission COHb level correlated with the severity of neuropsychiatric outcomes on sub-group analysis but the duration of CO exposure was not significantly associated with clinical outcomes.

Conclusion: Evidence has substantiated that hypoxic cerebral insult as a result of CO poisoning is not uncommon in survivors who are presented with variable neuropsychiatric outcome. These survivors may require further specialist care and attention in view of their residual neuropsychiatric deficit. Further study may be required to clarify these findings.

Partial Anterior Circulatory Ischaemic Infarct: a Prospective Study of 20 Patients with First-ever Stroke

D 8

MH Fu, CM Chang
Integrated Medical Services, Ruttonjee Hospital, Hong Kong SAR

Background: A detailed study on total anterior circulation infarct was reported by us in 2003 but no such study on partial anterior circulation infarct had been done in Hong Kong before.

Methods: Twenty first-ever stroke patients presenting with the partial anterior circulatory infarct (PACI) syndrome were identified according to the Oxfordshire Community Stroke Project classification. The syndrome was confirmed by two brain computed tomograms performed on admission and 10 days later. Patient demographics were collected. The Glasgow Coma Scale and the National Institutes of Health Stroke Scale were used to assess stroke severity on admission. Electrocardiography, transthoracic echocardiography, duplex ultrasound of extracranial carotid arteries, transcranial doppler ultrasound of intracranial arteries, and/or magnetic resonance arteriography were performed to study the underlying stroke mechanisms. A stroke mechanism was assigned to each patient according to the TOAST classification. In-hospital treatments and complications were recorded. Outcome was assessed 1 month, 3 months, and 1 year after stroke, using the modified Rankin Scale and the National Institutes of Health Stroke Scale.

Results: Seven patients had large striatocapsular infarct, six had medium-sized cortical infarct, five had borderzone cortical infarct, and two had small cortical infarct. The underlying stroke mechanisms were large artery atherosclerosis in one patient, cardioembolism in five patients, and undetermined aetiology in 14 patients (no cause found despite complete evaluation in 10, incomplete evaluation in 2, multiple potential stroke mechanisms in 2). Recurrent ischaemic stroke occurred early in two patients and late in one patient. Although there was no death at 3 months and only one late vascular-related death, 12 and 8 patients were still functionally dependent at 3 months and 1 year, respectively.

Conclusion: Standard investigations still cannot determine the underlying stroke mechanism in about half of local Chinese patients suffering from PACI. For those with a determined cause, cardioembolism seemed to be more common than large artery atherosclerosis. Although stroke-related mortality was very low, the chance of early recurrence was substantial and permanent functional disability was present in a significant proportion of PACI patients.

WL Ng

United Christian Hospital, Hong Kong SAR

Idiopathic inflammatory myopathies (IIM) are a group of acquired and potentially treatable myopathies. On the basis of unique clinical, histopathological, immunological, and demographic features, they can be differentiated into three major and distinct subsets: dermatomyositis (DM), polymyositis (PM), and inclusion-body myositis (IBM). This review focuses on the first two conditions. Though the classical presentation of proximal myopathy with elevation of muscle enzymes is readily recognisable, especially if accompanied by characteristic dermatologic features in case of DM, diagnosis in real life may prove elusive.

The degree of muscle weakness may vary at presentation and clinical picture could be confounded and overshadowed by other manifestations including arthritis, weight loss, malaise, or finding of elevated 'transaminases'. Diagnostic workup may be misdirected towards rheumatoid arthritis, systemic lupus erythematosus, dysthyroidism, malignancies, or even hepatitis. Early recognition requires awareness and alertness among family practitioners, emergency care physicians, and general internists.

The full diagnostic workup should include a comprehensive evaluation of the extent and severity of muscular weakness, including the involvement of oropharyngeal and oesophageal muscles. Lung involvement is an important complication. Most patients have a chronic indolent course with relatively favourable prognosis but a rapidly progressive form of interstitial pneumonitis with high mortality is being increasingly recognised.

Dermatomyositis and to a lesser extent PM are known to be associated with underlying malignancy. The spectrum of malignancies parallels the distribution in the general population with over-representation of cervical, lung, gastro-intestinal cancers, and non-Hodgkin's lymphoma. Local data concur with worldwide experience except that nasopharyngeal carcinoma is among the most frequently associated malignancy.

Early diagnosis and timely initiation of therapy is essential, since both DM and PM respond better to early commencement of immunotherapeutic agents. Corticosteroids are the cornerstone of therapy but often require combination with second-line agents such as methotrexate or azathioprine to induce or sustain a clinical remission. New immunomodulatory agents including calcineurin inhibitors and mycophenolate mofetil have reports of success. Biologic agents such as tumour necrosis factor- α and rituximab are currently being tested in controlled trials. Attention should also be paid to the management of pre-existing or iatrogenic cardiovascular co-morbidities such as diabetes mellitus and hypertension. Measures should be taken to minimise treatment-related complications including infections and osteoporosis. A multi-disciplinary team approach involving experienced physicians, physical therapists, speech therapists, and dietitians is pivotal.

George Karpati

Montreal Neurological Institute, Quebec, Canada

This presentation will provide up-to-date information about the following topics:

1. Definitions of molecular medicine, molecular neurology, and molecular myology.
2. The impact and significance of molecular myology to be presented under the following headings:

- Understanding disease pathophysiology
- Rational classification
- Investigation and precise diagnosis
- Therapy and prevention
- Genetic counselling
- Ethical aspects
- Research

Particular emphasis will be placed on the discussion of pathophysiology, therapy, and ethical aspects.

3. In the category of pathophysiology, description will be presented and illustrated regarding a dominant disease (myotonic dystrophy 1 [Myd 1]) and a recessive disease (Duchenne dystrophy [DMD]) and mitochondrial myopathies.
4. Regarding molecular therapies and cell therapies, the following modalities will be discussed:
 - A. Recessive diseases using DMD as a prototype:
 - Gene replacement
 - Upregulating a compensating molecule
 - Gene correction (DNA editing)
 - Primary transcript correction ("exon skipping")
 - Translational manipulation ("read-through")
 - Myostatin inhibition
 - B. Dominant diseases using Myd 1 as a prototype:
 - Blocking the mutant mRNA by antisense oligonucleotides
 - Inactivation of the mutant mRNA by RNAi
 - Upregulating muscle bind protein 1 (Myd 1) to restore splicing accuracy
 - C. Cell therapies:
 - Myogenic progenitor cells (satellite cells)
 - Adult myogenic stem cells
 - Mesangioblasts
 - Embryonic stem cells
5. Ethical issues particularly in relation to molecular therapies will be dissected.

Jun Kimura

University of Iowa, Iowa, United States

Conventional nerve conduction studies help document the site of a focal lesion within a segment flanked by two successive stimuli, usually 10 to 20 cm apart. A focal lesion tends to escape detection if evaluated along a longer course of the nerve because the inclusion of the unaffected segments dilutes the effect of restricted slowing, lowering the sensitivity. Thus, inching the stimulus in shorter increments in the range of one to several cms allows more precise localisation required to isolate the exact site of involvement within the affected segment.

In contrast, long distances, although insensitive to focal lesions, provide better yields for a diffuse or multisegmental process. Evaluation of a longer segment by means of F wave provides an excellent measure for assessing a diffuse or multi-segmental process such as polyneuropathies. A longer path tends to accumulate segmental or diffuse abnormalities, which collectively show a clear deviation from the normal range. In addition, evaluating a longer segment also improves overall accuracy in measuring the distance and latency because the same absolute error constitutes a smaller percentage change when compared to a shorter segment.

Nerve conduction studies supplement clinical observation by characterising the conduction changes and delineating the extent and distribution of the neural abnormalities. The type of lesions under consideration dictates proper choice of techniques that help quantitate the degree of involvement for optimal results. Thus, physiological studies become a reliable means of testing peripheral nerve function if conducted as an extension of the clinical examination rather than a laboratory test.

Individualising Antiepileptic Drug Therapy for Patients with Epilepsy

Kore Liow

Via Christi Comprehensive Epilepsy Center, Kansas, United States

Since 1979, many 'second generation' antiepileptic drugs (AEDs) have been approved and available for the treatment of epilepsy, thus making the selection of AEDs for patients with epilepsy more complex than ever before. To individualise the treatment options, it is important to (1) make an accurate diagnosis, (2) maximise the use of AEDs, (3) think outside the box.

Accurate diagnosis of epilepsy starts with ruling out other causes of nonepileptic events, followed by classifying the seizure type and syndrome with the help of a good history, examination, electroencephalograms, and neuroimaging.

Maximising the use of AEDs will require a clear understanding of the pharmacokinetics and drug interactions of each AED; favourable characteristics include AEDs with no drug interactions and which does not induce the P450 enzyme system. Selection can also be based on the unique side-effects of the various AEDs, based on patient lifestyle and preferences. Antiepileptic drugs can also be selected based on whether a co-existing condition like migraine or neuropathy is present. Special consideration is given to female patients of childbearing age and the elderly.

'Thinking outside of the box' means paying attention to the psychological and social impact of epilepsy on the patients and their family. Consider referring the patients to a specialised epilepsy centre where a team approach might benefit them including evaluation for epilepsy surgery and implantation of neurodevice.

Patrick Kwan

Prince of Wales Hospital, Hong Kong SAR

Pharmacogenomics is the study of the entire spectrum of genetic determination of drug response. This includes drug response profiles, drug discovery, and drug development based on knowledge of the human genome, as well as the effect of drugs on gene expression. It promises the prescription of 'the right drug for the right patient'.

It is a rapidly developing area of interest as more and more scientists are realising that genetic differences can contribute to interindividual variations in drug toxicity and efficacy. The completion of the human genome and the HapMap projects offers opportunities for accelerated research in this arena.

In the field of epilepsy, it is well-established that polymorphisms of the hepatic cytochrome P450 enzymes CYP2C9 and 2C19 can affect the clearance of phenytoin and phenobarbital, respectively.¹ There are recent reports by independent groups of investigators that the HLA-B*1502 allele is strongly associated with severe cutaneous reactions to carbamazepine in Chinese populations.^{2,3}

Recent attention has turned to the possible effect of genetic variations on drug efficacy. Accumulating evidence suggests that cerebral access of certain antiepileptic drugs is limited by drug transporters at the blood-brain barrier, the prototype of which is P-glycoprotein.⁴ There are conflicting reports whether polymorphisms of the *ABCB1* gene, which encodes P-glycoprotein, affect the level of protein expression and are associated with resistance to antiepileptic drug therapy.⁵

As a growing discipline, pharmacogenomics in epilepsy faces tremendous challenges in both research and clinical application. These include phenotype definitions, research methodology, statistical power, ethnic variations, as well as a range of ethical considerations such as right to test, access, and use the genetic information.

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Acupuncture and Traditional Chinese Medicine for Epilepsy

S II-6

Daniel KL Cheuk

Queen Mary Hospital, Hong Kong SAR

Traditional Chinese medicine (TCM) has unique theories regarding aetiology, diagnosis, and treatment of diseases. The TCM diagnostic pattern (ie inspection, listening, smelling, inquiry, and palpation) follows a completely different rationale compared to western medicine. In China, "epilepsy" first appeared in Huang Di Nei Ching, written in about 770-221 B.C. The description of epilepsy in this book and in many others was confined to generalised convulsive seizures, without documentation of absence or simple partial seizures. The treatment of epilepsy, based on principles of "Yin Yang Wu Xing", consisted of acupuncture, herbs, massage, food therapy, and therapeutic exercise.

Acupuncture is a procedure in which specific body areas, the meridian points, are pierced with fine needles. Variants of acupuncture include electroacupuncture, laser acupuncture, and acupressure. Studies have demonstrated that acupuncture can cause multiple biological responses, mediated mainly by sensory neurons to many structures in the central nervous system. Acupuncture may inhibit seizures partly by increasing the release of inhibitory neurotransmitters such as serotonin, GABA, or opioid peptides. However, a Cochrane review of randomised controlled trials concluded that the current evidence does not support acupuncture for treatment of epilepsy. Much larger, high-quality clinical trials are needed to further investigate the benefits of acupuncture in patients with epilepsy.

Traditional Chinese medicine herbs that have been found to have anti-convulsive effects by experimental research include *Uncaria rhynchophylla*, *Shitei-To*, *Qingyangshen*, *Tianma* (gastrodia rhizome), *Changpu* (*Acorus calamus*), and *Dannanxing* (bile arisaema), etc. Although the active ingredient is not known for each herb, there are human and animal studies that suggest their anti-convulsant effects. However, the benefits and adverse reactions of these treatments have not been systematically reviewed. A group of Cochrane reviewers has produced a protocol for systematic review on the comparative effectiveness and safety of TCM for treating epilepsy. A final review with recommendations is expected in the near future.

Neurology of the Chinese Language

S III-7

Chen-ya Huang

President, Hong Kong Neurological Society (1983-86), Hong Kong SAR

Chinese differs from European languages in that it is a tonal language, and has orthography which is processed differently from an alphabetical language, as the pronunciation is related to the visual code differently. This presents the neurologist with a fascinating area of research which is however under-explored. We review here recent literature on some basic and clinical neurolinguistic findings, which suggest that the classical European model for language representation in the central nervous system is modified by the difference in linguistic properties, and this has implication for clinical presentation and rehabilitation.

Writing for Medical Journals

S III-8

Richard Kay

President, Hong Kong Neurological Society (1990-92), Hong Kong SAR

Editors of general medical journals face similar challenges. On the one hand, they want their journals to be respected by the scientific community, and on the other, they want their journals to be enjoyed by the broader readership. They all need to strike a balance between the number of submissions they receive and the number of articles they publish.

Most journals operate a system of initial in-house screening of submitted manuscripts before sending them out for review. Editors treat their reviewers with utmost respect (because they are precious) and will rarely act against their advice. If the reviewer points out more than a few problems with a manuscript, the editor is more likely to reject it than to ask the author to fix these problems. Common fatal problems include lack of novelty, lack of relevance, poor science or statistics, and inappropriate conclusions.

Poor English is not necessarily a killer, but good English always help. At least, the reviewer would not complain (which they often do). Every journal has a certain style which you can follow by reading through some previous issues. Figures and tables will make your manuscript more acceptable but they must be well made and not in excess of the numbers allowed.

If your paper is rejected, you can consider appealing. Most journals don't mention this possibility, but it works! Otherwise, resubmit to a less competitive journal as quickly as possible.

Medicolegal Work for Neurologists

S III-9

YL Yu

President, Hong Kong Neurological Society (1986-88), Hong Kong SAR

Neurologists often come across work of a medicolegal nature. The major reasons include: frequent occurrence of permanent impairments as a result of lesions in the nervous system; difficulty in diagnosing certain neurological disorders for non-neurologists; and increased awareness of patient's rights. In general there are four categories:

1. As attending physician providing a report on facts relating to patient care—clear documentation of the events and findings forms the basis of the report. Opinion about causation and impairment assessment is not required.
2. Medical negligence—the test to be applied is of reasonable standard and not of ideal standard. Beware of outcome bias.
3. Assessment of quantum—insult to the brain, spinal cord, and peripheral nerves brings special pattern of impairments. Amplification of symptoms and disabilities is often encountered. The Guides to the Evaluation of Permanent Impairment (AMA Guides) are widely used in the assessment of impairments.
4. Testamentary capacity—the mental ability to understand and execute legal documents.

Illustrative cases and cautionary tales will be discussed.

George Karpati

Montreal Neurological Institute, Quebec, Canada

This presentation concerns various modalities of molecular therapies for the nervous system and muscle that are in the stages of either preclinical experimentation or early clinical trials.

Molecular therapies include two general categories, each of which is designed to mitigate or negate the deleterious pathogenic effects in a disease:

1. Application of genetic material ('gene therapy')
2. Application of non-genetic compounds which, however, may eliminate deleterious gene expression ('genetic therapy').

Diseases amenable for molecular therapy may be genetically determined or non-genetic diseases. In the genetic category, we can distinguish different methods that are suitable to control either recessive or dominant diseases. The methods for recessive diseases include gene transfer for gene replacement, or specific modifications of the primary transcript (ie exon skipping, etc). For dominant diseases the main aim is to neutralise the dominant negative mRNA originating from one allele of a gene by such methods as application of specific interfering RNA or antisense oligonucleotides.

In the category of genetic therapies, examples include the application of compounds that upregulate a synergist of a molecule missing in a disease (ie utrophin in dystrophinopathies), or the use of a molecule coded PTC124 which induces translational readthrough of stop codons.

Non-genetic diseases that are treatable with molecular therapies include degenerative central nervous system diseases in which a stable gene reservoir for a trophic substance or for a particular neurotransmitter or neuromodulator can be beneficial. Parkinson's disease and Alzheimer's disease will be discussed in detail in view of their great importance in neurological practice. Neoplastic diseases constitute another group in this category.

Vincent Mok

Prince of Wales Hospital, Hong Kong SAR

Subcortical ischaemic vascular disease (SIVD) refers to arteriosclerosis affecting cerebral penetrating small arteries resulting in lacune, white matter lesion (WML), and/or microbleeds (MBs)¹ affecting the subcortical brain region. Lacunar stroke is as common as intracranial large artery disease in Chinese, accounting for 30% of ischaemic stroke.^{2,3} Varying severity of WML is seen in 80%⁴ of those with lacunar stroke and 30% of those stroke-free subjects with multiple vascular risk factors in Chinese.⁵ SIVD is the commonest subtype of vascular dementia. The mechanism whereby SIVD induces cognitive impairment or dementia is complex, and may involve an interplay of the host factors (eg age, education, genetic), severity and site of the ischaemic lesions, global, cortical, and/or regional brain atrophy, and/or concurrent Alzheimer's pathology.^{4,6,7} Potential preventive treatments may include anti-platelet and anti-hypertensive agents. Post-hoc analyses on statins in retarding WML progression showed conflicting results.⁸ On-going study is evaluating homocysteine⁹ lowering therapy in slowing WML and cognitive progression. Symptomatic treatments using acetylcholinesterase inhibitors¹⁰ and memantine have shown at most only modest benefit.

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Vladimir Hachinski

University of Western Ontario, Ontario, Canada

The growing menace

8% of individuals over the age of 65 years have had a stroke, 8% are demented and 17% have some cognitive impairment short of dementia. Cognitive impairment and stroke represent risks for each other. 25% of those who have cognitive impairment have had a stroke and 64% of stroke patients have some cognitive impairment. One in four individuals aged 65 years or older will suffer a stroke, cognitive impairment or both, unless we do something about it.

Limitations of current approaches

Currently attention focuses on the extremes, patients with problems severe enough to come to medical attention, typically with a stroke or dementia. In between, lie the neglected majority of patients who may have silent cerebral infarcts, leukoaraiosis, subclinical or incipient Alzheimer's disease, and various combinations thereof. Stroke specialists evince little interest in cognitive disorders and those interested in cognitive disorders largely focus on Alzheimer's disease, showing little interest or expertise in cerebrovascular disorders. Current criteria for diagnosing cognitive disorders are woefully inadequate, and put the emphasis on the late stages at which time little can be done. We have suggested the term "vascular cognitive impairment" to identify any cognitive disorder caused by or associated with vascular factors, which in principle are treatable and preventable.

Developing a common approach

Physical inactivity, obesity, hypertension, and hyperlipidaemia represent risk factors for stroke and also for so-called Alzheimer's disease. We need to develop a common vocabulary of understanding and focus on disease mechanisms rather than nosological descriptions, identify common therapeutic targets and speed up the pace of preventive trials. Fortunately, the accelerating pace of scientific discovery, the power of electronic communication and growing awareness, offer opportunities to stem the tide of stroke and cognitive disorders. The wellbeing of millions depends on it.

Vladimir Hachinski

University of Western Ontario, Ontario, Canada

Stroke is the second commonest cause of death in the world and a leading and rising cause of death and disability in China.

The first World Stroke Day was proclaimed in Cape Town, 26 October 2006 on the theme "Stroke is a treatable and preventable catastrophe". A world agenda was set in the World Stroke Day Proclamation. It exhorts to:

1. Join forces to prevent stroke.
2. Ensure what we know becomes what is done.
3. Recognise the uniqueness of stroke.
4. Recognise, treat, and prevent vascular cognitive impairment.
5. Build transdisciplinary teams for stroke care and rehabilitation.
6. Actively engage the public around the world.

The two international stroke organisations, ie The International Stroke Society and the World Stroke Federation, have merged into a single World Stroke Organization (WSO) led by Geoffrey Donnan from Australia along with an international, elected Executive.

The World Federation of Neurology (WFN) through its Liaison Committee, which comprises a few of the world leaders in stroke, will try to coordinate all stroke activities worldwide and specifically oversee a yearly World Stroke Day, which this year will be on 9 October. One highlight was a press conference and special activities at the World Stroke Day during the XII Panamerican Congress of Neurology held in Santo Domingo, Dominican Republic, 8-12 October 2007. Another activity that the WFN, the WSO and the WHO are collaborating on, is the STEPS Stroke Surveillance Program led by Dr Ruth Bonita from the United States. A third activity is the coordination of stroke education in the developing world.

The Liaison Committee will endeavour to take an inventory of current stroke activities, evaluate their effectiveness and help develop an overall global strategy for stroke based on the World Stroke Day Proclamation.

The challenges have never been so formidable, but we have never been in a better position to do something about it. Let's do it!

Stanley Fahn

Columbia University Medical Center, New York, United States

There has been an explosion in basic science developments in Parkinson disease (PD), and the pace continues, so it is hard even for the expert to keep up. Clinical advances are only slightly less frenetic. Many of the clues on the aetiology and pathogenesis of PD come from genetic studies so that a number of monogenetic forms of PD are now known. PARK1 (SNCA), the gene for α -synuclein, continues to play an important role when PARK4 was discovered to be triplications and duplications of normal (wild-type) α -synuclein. Therefore, not just a mutation of α -synuclein can cause PD, but an increase in the amount of wild-type protein can. Accumulation of α -synuclein in Lewy bodies and Lewy neurites starts in the lower brainstem, not the substantia nigra (SN), and then progresses rostrally to eventually involve upper brainstem, mesocortex and neocortex. The *LRRK2* gene, though, has been found to be the most common mutation to cause PD and is present in up to 2% of sporadic cases, it is particularly prevalent in certain ethnic populations. Ideas have developed as to why the SN dopaminergic neurons are particularly vulnerable for degeneration.

Interest in neuroprotection has led to several randomised controlled trials. There have been winners and losers, and ideas for new agents are outpacing our ability to recruit subjects and finance these trials. Monoamine oxidase inhibitors have been successful in slowing clinical progression even in the presence of a strong symptomatic drug, levodopa. More powerful antioxidants are being developed and tested. So are drugs that block calcium channels to convert the autonomous firing of SNc dopaminergic neurons via the calcium channel in adults to their juvenile form of sodium conductance because intracellular calcium can enter mitochondria and disrupt this important cellular structure. Drugs that interfere with α -synuclein models of PD also have great potential.

Jonas Yeung

Alice Ho Miu Ling Nethersole Hospital, Hong Kong SAR

Deep brain stimulation (DBS) has been shown in medical research literatures to be effective in Parkinson's disease (PD), mainly in alleviating the dopamine-related symptoms and motor complications. It is also effective in dystonia, especially DYT1 dystonia and tardive dystonia. The first patient receiving DBS in Hong Kong was in 1997, with underlying diagnosis of PD with prominent tremor. The DBS target was at ventrointermedius (VIM) thalamic nucleus, and the clinical outcome was strikingly beneficial. Up till August 2007, there were a total of 96 patients receiving DBS in Hong Kong (46 male, 50 female). Diagnoses of underlying disease include: PD (89), tremor related to haemorrhage from arteriovenous malformation (1), manganism (1), and dystonia (5). The choice of target for DBS was initially thalamus VIM nucleus. Eventually mainly subthalamic nucleus was employed for PD, and globus pallidus interna was selected for dystonia and less so for PD. Target mapping was by combining information from magnetic resonance imaging, microelectrode recording and intra-operative clinical evaluation of signs and symptoms. Initially unilateral DBS was performed, but analysis of data showed significant interside imbalance of requirement of levodopa and dyskinesia threshold. Therefore bilateral DBS within same operation was the preferred strategy. The clinical outcomes for DBS in PD locally had been shown to be satisfactory, with results comparable to published data. Results for dystonia patients (DYT1 and tardive dystonia) were similarly satisfactory. There was no mortality peri- or post-operatively. Complications included cerebral haemorrhage, lead malposition, lead migration, lead fracture, infection at site of implantable pulse generator. Future challenges ahead include DBS targeting at pedunculopontine nucleus for improving gait dysfunction, as well as other neurological diseases.

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