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40th MEETING OF THE

Canadian Congress of Neurological Sciences

OTTAWA, ONTARIO JUNE 14-18, 2005

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40th meeting of the Canadian Congress of Neurological Sciences

Tuesday, June 14th, 2005

08:00-17:30 Neurobiology Review Course
08:30-16:00 ALS Strategies for Quality Life/Quality Care
19:00-21:00 Movement Disorders Video Session
19:00-21:00 Epilepsy Video Session

Wednesday, June 15th, 2005

07:45-17:00 Complex Spinal Neurosurgery Course
08:00-12:00 Consensus and Controversies in Epilepsy
08:00-12:00 EMG – Neuromuscular Disorders and EMG Crossfire
08:00-12:00 Neuroanatomy Refresher Course
13:30-17:30 Principles and Clinical Applications of EEG and Evoked Potentials
13:30-17:30 Current Standards and Advances in Neuro-Imaging for Treatment of Brain Tumours
13:30-17:30 MRI Course in Neurology
13:30-17:30 Waking up to the Importance of Sleep Disorders
18:00-20:00 Welcome Reception

Thursday, June 16th, 2005

08:30-10:30 Plenary Session I – Topics on Peripheral Nerve Function, Disease and Repair
11:00-13:00 Platform Sessions
11:00-19:00 Exhibits/Poster Sessions
14:30-16:00 Platform Sessions
16:00-17:30 Grand Rounds
19:00-21:00 Mild Cognitive Impairment: The Border Zone Between Normality and Dementia

Friday, June 17, 2005

08:30-10:30 Plenary Session II – Leaders in Canadian Neuroscience
10:00-15:00 Exhibits/Poster Sessions
11:00-13:00 Platform Sessions
14:30-16:30 Plenary Session III – Joint Session with Canadian Association of Physical Medicine and Rehabilitation: Perspectives on neuromuscular disease
18:30-20:30 Jazz, Art and Architecture Reception

Saturday, June 18th, 2005

08:00-10:00 Mini-symposia
What's New in the Clinical Neurosciences
Maximizing CME/CPD Opportunities
Neurocritical Care – Contemporary Issues in the Diagnosis and Management of Typical NICU Cases
08:30-17:00 Advances in the Diagnosis and Treatment of Pediatric Neuromuscular Diseases
10:30-17:30 Stroke Prevention 2005
10:30-17:30 Contemporary Issues in Multiple Sclerosis

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ABSTRACTS

SOCIETY PRIZE PRESENTATIONS

Canadian Association of Child Neurology – President's Prize
Canadian Neurological Society – Frances McNaughton Memorial Prize
Canadian Neurosurgical Society – K.G. McKenzie Prize in Basic Neuroscience Research
Canadian Neurosurgical Society – K.G. McKenzie Prize in Clinical Neuroscience Research
Canadian Neurological Society – Andre Barbeau Prize

PLATFORM PRESENTATIONS

Thursday June 16, 2005

Friday June 17, 2005

POSTER PRESENTATIONS

Wednesday June 15, 2005 to Friday June 17, 2005
Special Poster Tours June 16, 2005 - 17:30 - 19:00

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2005 Society Prize Papers

The President's Prize – Canadian Association of Child Neurology

Autosomal recessive cerebellar hypoplasia in the Hutterite population: A syndrome of nonprogressive cerebellar ataxia with mental retardation

HC Glass (Calgary), KM Boycott (Calgary), C Adams (Victoria), K Barlow (Calgary), J Scott (Calgary), AE Chudley (Winnipeg), TM Fujiwara (Montreal), K Morgan (Montreal), E Wirrell (Calgary), DR McLeod (Calgary)*

Background: Cerebellar hypoplasia is a rare malformation with a number of underlying causes. It typically manifests clinically as non-progressive cerebellar ataxia with or without mental handicap. We further describe a syndrome of autosomal recessive cerebellar hypoplasia that has been recognized in the Hutterite population and referred to as the dysequilibrium syndrome (DES-H). *Methods:* We reviewed 12 patients with this syndrome ranging in age from four to 33 years. Subjects were examined and underwent a standard set of investigations, including magnetic resonance imaging, to better characterize the clinical features, natural history and neuroimaging. *Results:* DES-H is an autosomal recessive disorder with distinct clinical features including global developmental delay, late ambulation (after age six), truncal ataxia and a static clinical course. The neuroimaging is characterized by hypoplasia of the inferior portion of the cerebellar hemispheres and vermis and mild simplification of cortical gyri. *Conclusions:* Characterization of the Hutterite disequilibrium syndrome allows better classification of this syndrome among the cerebellar hypoplasias. This isolated population will be important for future mapping and gene identification projects, and will ultimately contribute to the understanding of human brain development.

Frances McNaughton Memorial Prize – Canadian Neurological Society

Sensory neuropathy in HIV/AIDS patients highly exposed to antiretroviral therapy: protease inhibitor-mediated neurotoxicity

JA Pettersen (Calgary), G Jones (Calgary), C Worthington (Calgary), HB Krentz (Calgary), OT Keppler (Heidelburg), A Hoke (Baltimore), MJ Gill (Calgary), C Power (Calgary)*

Background: HIV-sensory neuropathy (HIV-SN) is a common, disabling syndrome affecting HIV-infected patients. Our principal objective was to define its clinical determinants, including the role of antiretroviral therapy (ART). *Methods:* We performed longitudinal analyses of an HIV-infected cohort with neurological diseases, prospectively identifying patients with and without HIV-SN. Cumulative dosages and durations of exposure to ARTs were examined with demographic and clinical data. Sensory neuron injury was assessed with and without ARTs in rat dorsal root ganglia (DRG) cultures transgenic for human CD4 and CCR5 and infected with HIV-1. *Results:* Clinical Investigations. 221 HIV-positive patients were assessed from 1998-2004: 120 (54%) showed no evidence of HIV-SN; 101 (46%) exhibited HIV-SN [64 (29%) had distal-sensory-polyneuropathy (DSP); 37 (17%) had antiretroviral-toxic-neuropathy (ATN)]. Compared to non-neuropathy patients, HIV-SN patients were significantly older, showed higher mean-peak-viral loads, lower health-related-quality-of-life scores and had greater exposure to neurotoxic dideoxynucleosides and protease inhibitors (PIs) prior to HIV-SN. Laboratory Investigations. Treatment of HIV-infected, cultured DRGs with indinavir or didanosine produced significantly greater neuronal atrophy, neurite retraction and process loss compared to uninfected or untreated cultures. *Conclusions:* Exposure to PIs is a previously unrecognized risk factor for the development of HIV-SN. Given the widespread, protracted use of PIs, greater attention to these neurotoxic effects is warranted.

K.G. McKenzie Prizes in Basic Neuroscience Research – Canadian Neurosurgical Society

Regulation of glial cell polarity and invasion by Drr1

K Petrecca (Montreal), R Waldkircher (Montreal), A Angers-Loustau (Montreal), J Wang (Montreal), R Del Maestro (Montreal)*

Background: Tumors of glial origin consist of a central core mass and a peripheral front of invasive cells that are detectable up to several centimeters away from the core lesion. This invasion is a major factor in the aggressiveness of glial tumors and is often responsible for the failure of their treatment. *Material and Methods:* We designed an unbiased, genome-wide functional screen solely on the basis of glioma invasion in an attempt to identify invasion-associated genes. *Results:* Downregulated in renal cell carcinoma, Drr1, was identified in this screen as a candidate effector of invasion. It mediates hyperinvasion when overexpressed and significantly reduced invasion when expression is eliminated. Importantly, drr1 is highly expressed in invasive human gliomas whereas expression in normal human brain and noninvasive human gliomas is minimal. We also demonstrate that drr1 is a mediator of glial cell polarity using a pericentrin localization scratch assay. *Conclusions:* We have identified Drr1 as a potent regulator of glial cell invasion and cell polarity. Overexpression promotes glial cell invasion and enhanced cell polarity. Importantly, Drr1 is highly expressed in invasive gliomas. We propose enhanced cell polarity as a molecular mechanism underlying the aggressive nature of human gliomas that overexpress drr1.

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2005 Society Prize Papers

K.G. McKenzie Prizes in Clinical Neuroscience Research – Canadian Neurosurgical Society

The development and validation of a preoperative prediction score for chronic hydrocephalus in pediatric patients with posterior fossa tumors

*J Riva-Cambrin * (Toronto), M Lamberti-Pasculli (Toronto), M Sargent (Toronto), D Armstrong (Toronto), R Moineddin (Toronto) D Cochrane (Toronto), J Drake (Toronto)*

Introduction: Approximately 30% of pediatric patients with posterior fossa tumors develop chronic hydrocephalus. In most centers, expectant care is the current management of hydrocephalus for this population. There is some literature which suggests that permanent preoperative CSF diversion would diminish morbidity and hospital length of stay in 'high-risk' children. A validated prediction score would allow for tailoring and, thus, optimization of the care of these children. *Methods:* A literature search and formal qualitative interviews of leading experts in the field were used to generate meaningful potential predictors. Data from 343 patients (1988-2003) from HSC, Toronto was used to construct a prediction model and score. The model was applied to 111 patients (1988-2003) from BC Childrens Hospital, Vancouver to score each patient and these were statistically compared to whether CSF diversion was required. *Results:* Significant preoperative predictors of chronic hydrocephalus were age<2 (score=3), papilledema (score=1), qualitative radiological hydrocephalus severity (score=2), cerebral metastatic spread (score=3), and estimated tumor pathology by preoperative imaging (score=1). A score of 5/10 or higher is considered 'High Risk'. The score was clinically and statistically validated on an independent cohort (p-value of 0.0486; percent misclassification of only 20.7% (23/111)). *Discussion:* This score can safely and effectively be used to predict a patient's individual risk of chronic hydrocephalus, preoperatively discriminate between 'High Risk' patients and 'Low Risk' groups, and this effectiveness is generalizable across differing centres.

Andre Barbeau Memorial Prize – Canadian Neurological Society

Linear transform from epileptic spikes to BOLD fMRI signals in an animal model of occipital epilepsy

SM Mirsattari (London), Z Wang (London), JR Ives (London), F Bihari (London), LS Leung (London), R Bartha (London), RS Menon (London)*

Background: It is not known if the neurovascular coupling is maintained in an epileptic focus. This study aims to characterize the hemodynamic changes that accompany interictal epileptiform discharges (IEDs) in an animal model of occipital epilepsy using simultaneous electroencephalograph (EEG)-Blood Oxygenation-Level Dependent (BOLD) functional magnetic resonance imaging (fMRI). *Methods:* Three male adult Sprague-Dawley rats were anesthetized with inhalational isoflurane, immobilized in an MRI-compatible stereotactic frame and were injected with 0.2 _L of 100 units of sodium penicillin G in the right primary visual cortex. T2*-weighted MR images were acquired in 4T using a gradient-recalled EPI pulse sequence (TE/TR=10/200 ms, flip angle ~30^{O}, FOV 5cm, single slice 2mm, matrix size 128´128). Simultaneous EEG-fMRI data were recorded for 12 to 20 minutes during IEDs and divided into seven equal segments of 100 s for further analysis. Temporal independent component analysis (ICA) of EEG and spatial ICA of EPI data were analyzed simultaneously to generate spatial activation maps (t-statistics) thresholded at p<10-3 and overlaid on T1-weighted coronal anatomical images. *Results:* There was a significant coupling between BOLD signals and IEDs (cc=0.37-0.52). The ipsilateral occipital cortex and contralateral visual association cortices were activated during IEDs. *Conclusions:* Consistent increase in BOLD signals during IEDs is supportive of a preserved neurovascular coupling in the epileptic focus.

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Platform Presentations

Cerebrovascular Surgery

A-01

Biological response to eClips leaf coverings

J Spears (Toronto), T Gunnarsson (Toronto), B Qiang (Toronto), G Bourne (Vancouver), K Pritzker (Toronto), D Ricci (Toronto), I Penn (Toronto), T Marotta (Toronto)*

Background: Controlled re-endothelialization is the goal of endovascular closure of an intracranial aneurysm. This project was conducted to determine the biological reaction of various coverings on endovascular devices, including a novel device, eCLIPs (endovascular clip systems). *Methods:* Using a rabbit model, control stents (stainless steel), bare eClips (stainless steel) or polymer coated stents were deployed. Polymers studied included: silicone, silicone with phosphorylcholine, polyurethane, polyurethane with phosphorylcholine and Endexo.™ Histologic analysis and morphometric assessments included: quantitative vessel injury score and inflammation score. Student's t-test and analysis of variance (ANOVA) were performed. *Results:* The neointimal proliferation score for bare eClips showed no significant difference compared with controls ($p=0.497$). Remaining groups showed significantly more neointimal proliferation ($p<0.01$). Silicone and silicone with phosphorylcholine coated stents showed more intimal proliferation than other coverings. The injury score of only the bare eClips was significantly lower than the control group ($p <0.0001$). All other groups demonstrated no significant difference. The inflammation score of bare eClips, polyurethane covered and Endexo covered stents showed no significant difference compared with the control group. Stents covered with silicone, silicone with phosphorylcholine, and polyurethane with phosphorylcholine were significantly higher than the control group ($p<0.0001$). *Conclusions:* These findings have implications in the choice of coverings for intracranial endovascular devices.

A-02

Combined coronary artery bypass grafting and carotid endarterectomy: the University of Alberta experience

*J M Findlay** (Edmonton), A Koshal (Edmonton), D Modry (Edmonton), S Wang (Edmonton)*

Background: We reviewed our experience with combined coronary artery bypass grafting (CABG) and carotid endarterectomy (CEA). *Patients and Procedures:* Patients requiring CABG who also had either symptomatic carotid stenosis or significant asymptomatic stenosis have been considered candidates CABG and CEA performed under the same anaesthetic. Carotid investigation has been based on the presence of prior neurological symptoms or a carotid bruit. *Results:* Between 1989 and 2004 81 combined procedures have been performed at the University of Alberta Hospital, out of a total of 9552 CABG procedures done over the same period (0.8% of CABG patients). Sixty (74%) have been men, the mean age 69 years, and 48 patients (59%) had symptomatic carotid stenosis. All patients had stenoses 70% or greater in severity. At 30 days there was one neurological complication, a retinal artery embolus causing monocular blindness in a patient who presented with symptomatic carotid and coronary disease, and there was one death due to heart failure. *Conclusion:* The 2% stroke or death rate in this series of patients undergoing combined CABG/CEA indicate that at our hospital this approach is safe and reduces long-term stroke risk.

A-03

Current trends in the management of ruptured intracranial aneurysms in Toronto following the International Subarachnoid Trial

J Spears (Toronto), T Jonas-Kimchi (Toronto), B Gray, M Cusimano (Toronto), L Noel de Tilly (Toronto), R Moulton (Toronto) , P Muller (Toronto), R Perrin (Toronto), W Tucker (Toronto), W Montanera (Toronto), T Marotta (Toronto)*

Background: The impact of the International Subarachnoid Trial (ISAT) on the current management of ruptured intracranial aneurysms in a large urban Canadian center is presented. Methods: Prospectively collected data from a large urban hospital (St. Michael's Hospital, Toronto, Ontario)with 2 interventional neuroradiologists and 6 neurosurgeons was reviewed. *Results:* In 2001 and 2002 the percentage of ruptured aneurysms treated with surgical clipping was 82% (94.9%- 2001; 69.4%- 2002) with the remainder being coiled 18% (5.1% -2001; 30.6%-2002). Following the release of ISAT, the number of ruptured intracranial aneurysms treated with GDC coiling for the years 2003 and 2004 increased to 35.6%. In 2004 alone, 51.6% of all ruptured intracranial aneurysms were treated with GDC coiling. The overall distribution of ruptured aneurysms treated with GDC coiling was: 75.7% anterior circulation; 24.3% posterior circulation. A total of 60.6% occurred in the midline (Anterior Communicating - 43.9%, Basilar- 16.7%) with the remainder being paramedian. 30.3% required the use of an assist device (21.2% balloon assist, 9.1% stent assist). An overall complication rate (technical/angiographic/intraop rupture, clinically silent) was 10.6% and 1.5% of procedures were aborted prior to deployment of any coils. Clinical complication rate was less than 1%. *Conclusion:* GDC coiling appears to have a continuously expanding role in the current treatment of ruptured intracranial aneurysms that is only likely to increase with continuing technical advances in endovascular devices.

A-04

The optimal management of unruptured intracranial aneurysms: A decision analysis comparing coiling, clipping, and observation.

C O'Kelly (Toronto), L Zinman (Toronto), M Krahn (Toronto), MC Wallace (Toronto)*

Background: Asymptomatic intracranial aneurysms may rupture resulting in significant morbidity and mortality. The optimal management strategy for unruptured aneurysms remains controversial. Options include observation, surgical clipping, and

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endovascular coiling. *Methods:* A decision tree was constructed to determine the preferred management of a cohort of 40-year old subjects with an asymptomatic unruptured 10 mm intradural aneurysm. A Markov model was used to determine the quality adjusted life years and life expectancy of the decision options: coiling, clipping, or observation of an unruptured aneurysm. Sensitivity analysis assessed the accuracy of the model and the effect of potential covariates. *Results:* The optimal treatment for the cohort of patients considered in this analysis was clipping of the unruptured aneurysm. This option was associated with an incremental QALY gain of 1.97 over coiling and 5.09 over observation. The analysis was sensitive to the annual rupture risk of the unruptured aneurysm, at a threshold of 0.6%, year. *Conclusions:* This study demonstrated that subjects with asymptomatic unruptured aneurysms should be treated rather than observed if their annual rupture risk is > 0.6% per year. Although both aneurysm clipping and coiling were found to be superior to observation, clipping provided the maximum incremental QALY gain.

A-05

Stent repair of craniocervical arterial injuries

G Redekop (Vancouver), D Graeb (Vancouver), C Haw (Vancouver), R Heran (Vancouver)*

Background: Blunt or penetrating trauma to craniocervical arteries can lead to massive bleeding, pseudoaneurysm formation, or ischemic stroke. Endovascular repair with stents or stent-grafts is an attractive treatment option due to its minimally invasive nature and the ability to preserve or restore anatomical continuity of injured vessels. *Methods:* Twenty-five patients with penetrating arterial trauma or dissection were treated with stents or covered stent-grafts. Thirteen (52%) had expanding pseudoaneurysms, seven (28%) had acute ischemia, and five (20%) had massive bleeding or high-flow arteriovenous fistulae. *Results:* Self-expanding or balloon-expandable stents and/or covered stent grafts were used with successful arterial repair accomplished in all cases. There were no procedural neurological or cardiovascular complications. Two patients with contra-indication to anticoagulation or antiplatelet therapy and symptomatic arterial injuries treated with covered stent grafts had stent thrombosis observed on early follow-up imaging, without neurological sequelae. One patient with a covered stent graft had asymptomatic, delayed occlusion after one year. There were no ischemic neurological events. *Conclusions:* Endovascular stent repair of penetrating arterial injuries and dissections presenting with acute ischemia can be accomplished rapidly and safely. Early and delayed thrombosis has been observed with covered stent grafts, and long-term antiplatelet therapy is recommended.

A-06

Retrospective analysis of transluminal angioplasty as a treatment of cerebral vasospasm

P Lavoie (Quebec), JL Gariepy (Quebec), JM Bouchard (Quebec), JF Turcotte (Quebec), G Milot (Quebec)*

Background: The morbidity and mortality rates associated with cerebral vasospasm remain high, despite breakthroughs in neurosurgical intensive care. In that context, transluminal angioplasty is considered as a valuable add-on treatment. *Methods:* The authors have analyzed the evolution and occurrence of neurological deficits and radiological stroke in 77 patients suffering from vasospasm as a result of spontaneous cerebral hemorrhage. Patients in the study were separated into 2 groups based on the use of angioplasty. The patient group who did not undergo angioplasty was subdivided further based on the diagnostic method and possibility of evaluating the vasospasm clinical implications. The group of patients having undergone angioplasty was subdivided further based on the timing of the procedure. *Results:* There was complete resolution of symptoms in 75% of the angioplasty patients, 66% of which occurred in less than 3 days and only one patient had a relapse; 30% of angioplasty patients compared to 44% of patients without angioplasty in whom vasopasms clinical implications cannot be evaluated presented neurological deficits at follow-up (p=0.02). Twenty-five percent (25%) of patients experiencing vasospasm in dilated vessels in less than 24 hours compared to 100% of patients experiencing vasospasm in dilated vessels after 24 hours registered a new CAV on CT (p=0.04). *Conclusions:* Angioplasty represents an efficient, lasting solution which should be used more quickly and consistently in patients with clinical vasospasm and probably also in some patients in whom vasospasm clinical implications cannot be evaluated.

A-07

Developing an animal model for synchrotron-based neurovascular research

L Ogieglo (Saskatoon), S Fiedler (Hamburg), L Allen (Saskatoon), S Corde (Grenoble), F Esteve (Grenoble), M Kelly (Saskatoon), G LeDuc (Grenoble), C Nemoz (Grenoble), E Schültke (Saskatoon), K Meguro (Saskatoon)*

The objective of this project was to develop an animal model to study the potential of synchrotron-supported intravenous K-edge digital subtraction angiography (KEDSA) as novel diagnostic tool for neurovascular pathology. *Methods:* Seven adult male New Zealand rabbits were used as experimental subjects for angiographic imaging of the basal cerebral circulation. Five animals were used to image the cerebro-vascular anatomy in healthy animals. In the two remaining animals, subarachnoid hemorrhage was induced by injecting 2 ml of arterial blood from an ear artery into the cisterna magna. Images were acquired after intravenous injection of iodine-based contrast agent with two different detectors, both in planar projection as well as in CT mode. The experiments were conducted at the beamline ID 17, ESRF, Grenoble, France. *Results:* The quality of the images obtained with KEDSA after intravenous injection of contrast agent was comparable with the quality of images obtained with conventional X-ray equipment after intra-arterial contrast injection.

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A-08

Aneurysmal surgery in the presence of angiographic vasospasm: an outcome assessment

Nancy McLaughlin (Montreal), Michel W Bojanowski (Montreal)*

Background: The timing of aneurysmal surgery for patients presenting within the period at risk for vasospasm (VS) is controversial. We reviewed our experience of surgically treated patients in the presence of angiographic VS. *Methods:* Retrospective review of patients presenting an aneurysmal SAH with angiographic VS operated between 1990-2004. Functional outcome was assessed using the Glasgow Outcome Scale. *Results:* Fifty patients with angiographic VS were analyzed. On admission, 60% were in good clinical grade; 26%, fair grade; 14%, poor grade. Surgery was performed 24 hours or less after angiography in 88% and 48 hours or less in 98%. Pre-operatively, 20% manifested clinical VS. Post-operatively, 84% presented angiographic VS and 26% clinical VS. Outcome was favorable in 92% of all patients. Although 90% with pre-operative clinical VS were in good or intermediate grade on admission, only 70% presented a favorable outcome. Mortality occurred in 2 patients presenting pre-operative early clinical VS. *Conclusion:* Aneurysmal surgery following SAH in the presence of asymptomatic pre-operative angiographic VS is not associated with an unfavorable outcome. Early surgery is not contra-indicated and might enable optimal treatment of VS. However, clinical VS, especially within 48 hours after SAH, might be associated with less favorable outcome.

PEDIATRICS

B-01

The development and validation of a preoperative prediction score for chronic hydrocephalus in pediatric patients with posterior fossa tumors

*J Riva-Cambrin * (Toronto), M Lamberti-Pasculli (Toronto), M Sargent (Toronto), D Armstrong (Toronto), R Moineddin (Toronto) D Cochrane (Toronto), J Drake (Toronto)*

The K.G. McKenzie Prize in Clinical Neuroscience Research winner - Canadian Neurosurgical Society (See page 6).

B-02

Autosomal recessive cerebellar hypoplasia in the Hutterite population: A syndrome of nonprogressive cerebellar ataxia with mental retardation

HC Glass (Calgary), KM Boycott (Calgary), C Adams (Victoria), K Barlow (Calgary), J Scott (Calgary), AE Chudley (Winnipeg), TM Fujiwara (Montreal), K Morgan (Montreal), E Wirrell (Calgary), DR McLeod (Calgary)*

The President's Prize winner - Canadian Association of Child Neurology (See page 5)

B-03

Recurrence of synostosis following surgery for isolated sagittal craniosynostosis

D Agrawal (Vancouver), P Steinbok (Vancouver), D Cochrane (Vancouver)*

Background: Recurrence rates of synostosis following surgery in non-syndromic single suture craniosynostosis are not known. The aim of this study was to obtain this information for children with isolated sagittal synostosis and assess possible association of recurrent synostosis with intracranial hypertension. *Methods:* Fifty-five consecutive children, who had surgery for isolated sagittal synostosis from 1987 to 2000 and had postoperative skull radiographs, were reviewed retrospectively. Symptoms suggestive of raised ICP were recorded and skull radiographs were assessed for sutural synostosis and copper beaten appearance. *Results:* Surgery involved a minimum of vertex and parietal craniectomies. The median age at surgery was 4.3 months (2.1 to 38.6 months). Mean follow up was 35 months (2 to 156 months). Thirty-nine (70.9 %) had refusion of the sagittal suture at follow up. Eleven (28.2%) children with resynostosis had symptoms consistent with raised ICP and of these, 10 (90.1 %) had copper beaten appearance on skull radiographs. *Conclusions:* There is a very high incidence of resynostosis in children after surgery for isolated sagittal craniosynostosis, and this may be associated with copper beaten appearance of the skull and symptoms suggestive of intracranial hypertension.

B-04

Intraoperative urodynamics in tethered cord syndrome. An analysis of an experience in 240 surgically treated patients.

D Muzumdar (Ottawa), M Vassilyadi (Ottawa), ECG Ventureyra (Ottawa)*

Background: Tethered cord syndrome is characterized by progressive spinal deformity, back and leg pain with a potential for grave neurourological implications. Intraoperative urodynamic monitoring is of profound value in assisting the neurosurgeon to preserve or improve urologic function during detethering of the spinal cord. *Methods:* The case records of 240 consecutive pediatric patients who underwent tethered cord release surgery over the past 23-year period (1981- 2004) were reviewed retrospectively. Intraoperative urodynamic study included monitoring of urinary bladder pressure curves and electromyography of the external anal sphincter. The clinical data including preoperative, intraoperative and postoperative urodynamics were correlated and analyzed with respect to postoperative outcome. Patients who underwent initial surgical closure for open neural tube defects at birth were excluded. *Results:* The clinical symptomatology and urodynamic parameters improved in 208 (87.1%) children who underwent successful spinal cord detethering. 78 (32.7%) patients who were incontinent preoperatively had a normal voiding pattern postoperatively. 128 (53.5%) patients were able to void without catheterization. In 2 (1%) patients, there was deterioration in urodynamic parameters. In 4 (2%) patients, urodynamic parameters prevented a complete untethering without a

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further decrease in urological function. *Conclusions:* Intraoperative urodyamic monitoring is a useful adjunct during tethered cord release surgery to preserve urologic function, prevent progression and permanency of neurological changes and urinary dysfunction.

B-05

Intraosseous infusion into the skull: potential application for the management of hydrocephalus

J Pugh (Edmonton), J Tyler (Edmonton), T Churchill (Edmonton), R Fox (Edmonton), K Aronyk (Edmonton)*

Background: Numerous sites have been utilized for the diversion and absorption of CSF, yet despite years of innovation, CSF shunt systems continue to have high complication rates. The calvarial diploë represents an alternative site for CSF diversion. The effectiveness of intraosseous infusion through calvarial diploë has never been explored. This research into a novel solution for the management of hydrocephalus could lead to a significant improvement in the treatment of this hydrodynamic disorder. *Materials and Methods:* 14 crossbred adult pigs received glucose or FITC-Dextran infusions into the calvarial diploë to study the systemic absorption from the skull in an acute animal model. Systemic uptake was determined from serial samples obtained from an indwelling central venous catheter. *Results:* Following injection of either tracer, delivery to the systemic circulation was demonstrated within 30 seconds. *Conclusion:* Current management of hydrocephalus is not based on recreating normal CSF flow patterns from the brain to the dural venous system, but rather introduces new and complex hydrodynamic factors on an already complicated hydrodynamic disorder. Intraosseous infusion through the skull may represent a potential pathway to divert and absorb CSF, creating a shunt system that better restores a physiologic condition for CSF absorption.

B-06

Molecular and immunohistochemical study of grey and white matter brain injuries following perinatal infection and anoxia.

A Larouche (Sherbrooke), M Roy (Sherbrooke), S Girard (Sherbrooke), H Kadhim (Bruxelles), G Sébire (Sherbrooke)*

Background: Antenatal infection and anoxia are the main pathogenic processes triggering grey and white matter injuries in the brain of human neonates. We used our original rat model of neonatal brain lesions to study the effect of infectious and hypoxic-ischemic (H/I) aggressions on neuronal apoptosis, and astrocytes and microglial proliferation. *Methods:* Infectious effect was produced by administrating lipopolysaccharide (LPS) intraperitoneally (ip) to pregnant rats from embryonic day 17 (E17) to E20. H/I was induced at postnatal day 1 (P1) by ligature of the right common carotid artery followed by exposure to hypoxia (8% O2) for 3.5 hours. Brain injuries were examined at P3 and P8. *Results:* Results showed that most of the neocortex lesions observed after exposure to hypoxia, endotoxin, or both, were apoptotic as showed by TUNEL test. The extent of neuronal cell injury in the brain of rats exposed to postnatal H/I was significantly increased by antenatal exposure to LPS. Experimental aggressions resulted in both microglial and astroglial proliferation in the white matter as demonstrated by immunohistochemistry using ED1 and GFAP staining. *Conclusions:* This animal model provides an experimental tool to study the role of anoxic and infectious processes in the pathophysiology of perinatal human brain lesions and subsequent cerebral palsy.

B-07

Saccades in children with Chiari type II malformation

M Salman (Winnipeg), J Sharpe (Toronto), M Eizenman (Toronto), L Lillakas (Toronto), T To (Toronto), C Westall (Toronto), M Steinbach (Toronto), M Dennis (Toronto)*

Background: Chiari type II malformation (CII) is a congenital anomaly of the cerebellum and brainstem associated with spina bifida. The cerebellum and brainstem are important structures for processing saccades. Saccades are important for optimal visual function. We investigated the effects of CII on saccades. *Methods:* Saccades were recorded in 21 participants with CII, aged 8-19 years using an infrared eye tracker. Thirty-nine typically developing children served as controls. Participants made saccades to horizontal and vertical target steps. Regression analyses were used to investigate the effects of spinal lesion level, number of shunt revisions, and presence of nystagmus in the CII group. *Results:* Saccadic gains, asymptotic peak velocities, and latencies did not differ between the control and CII groups ($p > 0.01$). Spinal lesion level, number of shunt revisions or presence of nystagmus did not affect any of the saccadic parameters. *Conclusion:* Saccades are not affected by CII. Neural coding of saccades is robust despite the anatomical deformity of CII. This implies functional integrity of the ocular motor vermis, fastigial nuclei and their brainstem projections in CII.

B-08

Perception of Epilepsy Compared to Other Chronic Diseases of Adolescents: Through a Teenager s Eyes

C Cheung (Toronto), E Wirrell (Calgary)*

Objective: Adolescent perception of physical and personality/behavioral impact of chronic illness was assessed to determine a) is there greater prejudice toward epilepsy than other chronic disease, b) do adolescents with chronic disease have less prejudice towards similarly affected peers with all, or just their specific chronic disease. *Design:* Cohort study *Setting:* Outpatient clinics of a tertiary care pediatric hospital *Participants:* Cognitively normal teens aged 13-18 without chronic disease (N=41) and with epilepsy (N=32), asthma (N=38), diabetes (N=21) and migraine (N=17). *Main Outcome Measures:* Perceived physical and personality/behavioral impact of 8 chronic diseases (epilepsy, asthma, diabetes, Down syndrome, arthritis, migraine, leukemia, HIV infection). *Results:* Epilepsy was perceived to have more adverse physical impact than all chronic illnesses except Down syndrome. It was more likely to be perceived to commonly cause mental handicap, injure the afflicted individual and bystanders and lead to death. Epilepsy was also perceived to have more negative personality/behavior impact particularly on behavior, honesty, popularity, adeptness at sports and fun. Significantly more adolescents' expressed reluctance to befriend peers with epilepsy both from their own and their perceived parental perspectives. Having a chronic disease did not generally alter adolescents'

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perceptions of peers with chronic disease. However cases with epilepsy ranked this disease to have less personality/behavioral impact than teens with other chronic diseases. *Conclusions:* Adolescents perceive epilepsy to have a greater physical and personality/behavioral impact than most chronic diseases. Educational efforts should focus on the "normality" of most persons with epilepsy, and emphasize the low risk of injury when proper first aide is followed.

Spine and Nerve

C-01

Endplate kyphosis after Bryan Cervical Disc replacement

Shee Yan Fong (Calgary), Steven Casha (Calgary), Stephan duPlessis (Calgary), John Hurlbert (Calgary)*

Background: The aim of the study is to investigate the factors leading to endplate kyphosis after Bryan Cervical Disc replacement. *Methods:* Prospective study of a consecutively enrolled cohort of patients treated using the Bryan Cervical Disc prosthesis. Ten patients, age 36-52, were treated from February to November 2004 for C5-6/C6-7 radiculopathy(5), myelopathy(2), and both(3). Static and dynamic radiographs were measured digitally to determine endplate and functional spinal unit (FSU) angles, endplate range of motion (ROM), disc and vertebral body heights. *Results:* The endplate angles became more kyphotic in 9 patients after surgery, with a mean angle of -7° (p=0.007, 95%CI -12.58° to -6.04°). This correlated with the reduction in the caudal vertebral posterior height relative to its anterior height after surgery (p=0.011, r2=0.575). The preoperative disc kyphosis/height did not predict postoperative kyphosis. The ROM /FSU remained unchanged after surgery, and there was no correlation between endplate kyphosis and clinical outcomes (NDI and SF36). *Conclusions:* 90% of patients with Bryan Cervical Disc prosthesis had focal endplate kyphosis possibly due to faulty intraoperative caudal endplate preparation, but despite this, disc arthroplasty still preserved motion, angle of the FSU, and overall spinal sagittal alignment, with 90% of patients achieving cervical lordosis after surgery.

C-02

Primary Sacral Tumors: Classification of En Bloc Resection Techniques and Outcome

D Fourney (Saskatoon), L Rhines (Houston), S Hentschel (Saskatoon), Z Gokaslan (Baltimore)*

Background: En bloc resection with adequate margins is the only curative treatment for most primary sacral malignancies. We present a novel classification of surgical techniques based on the level of nerve root sacrifice, and evaluate functional and oncological outcomes. *Methods:* Retrospective review of 29 patients with en bloc resection of primary sacral tumors at the University of Texas M. D. Anderson Cancer Center (1993-2002). *Results:* Chordoma was the most frequent tumor (16 cases). Midline sacral amputation was performed in 25 patients (8 low, 4 middle, 7 high and 5 total sacrectomies; 1 hemicorporectomy). Lateral sacrectomy was performed in 4 patients (2 unilateral excisions of the sacroiliac joint and 2 hemisacrectomies). Surgical margins were wide in 19 cases, marginal in 9 and intralesional in one. Type of sacrectomy correlated with characteristic functional outcomes (bladder, bowel and gait). Length of hospital stay was related to the extent of sacrectomy. Median disease-free survival for chordoma by Kaplan-Meier analysis was 68 months (95% CI, 46-90). *Conclusions:* Classification of sacral resection techniques by the level of nerve root transection is useful in predicting postoperative function and morbidity. Adequate surgical margins should not be compromised to preserve function when they are necessary to affect cure.

C-03

Surgical management of the adult tethered cord syndrome: indications, techniques and long term outcomes in a series of 60 patients

G Lee (Toronto), G Paradiso (Toronto), C Tator (Toronto), F Gentili (Toronto), E Massicotte (Toronto), M Fehlings (Toronto)*

Background: Adult TCS continues to pose a significant management challenge. To date, relatively few studies have reported on patient outcomes following neurosurgical intervention. *Methods:* Patients who underwent de-tethering surgery at the Toronto Western Hospital between August 1993 and 2004 were identified. Their clinical charts, operative records and follow-up data were reviewed. *Results:* De-tethering procedures were performed in 60 patients(age range17-72 years) for TCS of varying aetiologies. The most common tethering lesions were tight filum terminale(n=29), post-myelomeningocoele repair(n=15), lipomatous malformations(n=9), split cord malformation(n=4) and arachnoidal adhesions(n=3). Fifty-nine patients presented with progressive pain and/or neurological dysfunction. Most patients had bladder dysfunction at presentation. In each case, microsurgery was performed under multi-modality intra-operative neurophysiological monitoring. The most common complications encountered were CSF leak and infections. One patient experienced worsened foot weakness post-operatively. At a mean follow-up period of 41.5 months, majority of patients presenting with back(78%) and leg pain(83%) improved. Pre-operative motor weakness(64%) was more likely to improve than sensory deficits(45%). Overall, neurological status was improved/stabilized in 90% of patients. Subjective improvement in bladder function was noted in 50% of patients. *Conclusions:* Surgery for adult TCS is safe and effective for improving pain and neurological status in majority of patients.

C-04

Current concepts and trends in management of rheumatoid craniocervical junction disease.

M Fehlings (Toronto), R Gurgo (Toronto)*

Background: Rheumatoid arthritis (RA) affects about 1% of the population, and in 20-50% of cases, the spine is involved, most commonly the craniocervical junction complex (CCJ). This can cause spinal instability and compression. We describe the current concepts in the management of CCJ involvement of RA, and examine specifically if early C1-2 fusion can prevent progression of cervical spine rheumatoid disease. *Methods:* Cervical spine cases for rheumatoid disease at the Toronto Western Hospital from 1992-2004 are reviewed. Specifically, the trend towards posterior fixation alone

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is examined. The extent of progression of cervical spine disease of patients who underwent C1-2 posterior fusion is reviewed. *Results:* 50 patients with rheumatoid disease underwent surgery of the craniocervical junction. Specifically no patient who underwent a C1-2 fusion required further surgery. *Conclusion:* Early C1-2 fusion in rheumatoid patients, once radiological instability has been demonstrated, may prevent the development of atlanto-occpital and subaxial spinal disease thus avoiding the need for more extensive posterior fusion procedures or even anterior decompression procedures. The use of more effective (screw-based) instrumentation systems may be responsible for less revision surgery being required for occipitocervical fusion procedures.

C-05

Delayed reinnervation of denervated and inappropriately protected peripheral nerve stumps

R Midha (Calgary), QG Xu (Calgary), T Gordon (Edmonton)*

Background: Delayed repair of peripheral nerve injuries often results in poor motor functional recovery partially due to deconditioning of endoneurial pathways in the distal nerve before motor axons can regenerate. In this study, the temporal sequence of reinnervation is examined in motor, sensory, and non-protected nerve stumps. *Methods:* Using the rat femoral nerve, we protected distal endoneurial pathways of the saphenous nerve with either cross-suture of the quadriceps motor nerve (Group A) or re-suture of the saphenous nerve (Group B) to compare later motor regeneration into the "protected" saphenous nerve pathway to chronic denervation and "unprotected" saphenous nerve (Group C). After 8 weeks, the femoral nerve's motor branch was re-cut and sutured to the distal saphenous nerve to allow motor reinnervation. The quantitative assessment of reinnervation was carried out after 3 , 6, and 9 weeks, by distal nerve sampling for axon counts and retrogradely labelled motoneuron counts. *Results:* Significantly more myelinated axons reinnervated the motor (A) than sensory (B) and no protection (C) groups at 6 weeks. Axon numbers declined in all groups but at 9 weeks, there were still significantly more axons innervating the distal endoneurial pathway in A than in group C. At 3 and 6 weeks, there were approximately 50% more labelled femoral motoneurons in A than in the B and C groups. Counts in group B and C improved over time, and, by 9 weeks, were comparable in all 3 groups. *Conclusions:* We conclude that initial motor innervation biases distal endoneurial pathways to favour motor axonal regeneration and that reinnervation of inappropriately innervated or denervated nerves is considerably delayed.

C-06

Evaluation of nerve regeneration across a peripheral nerve gap using a collagen nerve conduit filled with a collagen-based biomaterial associated with different neurotrophins - preliminary results

R Caissie (Quebec), L Jacques (Montreal), PE Landry (Quebec), F Berthod (Quebec)*

Background: The clinical results with peripheral nerve repair depends on the mechanism and the severity of the injury. Although the Gold standard treatment for peripheral nerve gaps today is the autograft, nerve guide conduits have become one of the common strategies for repairing major nerve defects. *Methods:* The surgical protocol will result in the interposition of collagen-based nerve guide tubes, filled with a collagen matrix at the junctionnal gap of sectioned rat sciatic nerves. Three-dimensional controlled release of various substances imbedded in the matrix within the nerve guide tubes between the proximal and distal ends of nerve repair sites will be studied under 5 experimental and 2 control settings. The quantitative analysis or regenerated nerve fibers will be assessed through serial immunohistochemical analysis. Neurosensory recovery will be evaluated with the Neurometer. Functionnal motor reinnervation will be clinically tested with the "Walking track analysis" and "Relative gastrocnemius muscle weight" indexes, currently used for such purposes. *Results:* Our preliminary results will be presented at the congress. *Conclusion:* We assume that any advancement in the functional outcome of neural regeneration can lower the morbidity and change the current therapeutic modalities for iatrogenic, post-traumatic or neoplastic nerve lesions that require nerve repair.

C-07

Comparing in vivo functional cervical spine motion following single level anterior cervical discectomy and fusion versus implantation of an artificial cervical disc

D Rabin (London), G Pickett (Manchester), N Duggal (London)*

Background: Anterior cervical discectomy and fusion (ACDF) for management of cervical spondylosis may accelerate further degenerative changes secondary to abnormal spinal motion, whereas cervical arthroplasty aims to maintain normal motion. This case-control retrospective study compared in vivo functional spinal motion in ACDF and artificial disc (AD) patients. *Methods:* Ten single-level AD patients were matched to single-level ACDF patients based on age, sex and level of surgery. Pre- and postoperative neutral and dynamic cervical radiographs were analyzed to determine sagittal range of motion (ROM), translation, change in disc height and center of rotation for all spinal units. *Results:* ROM at the operated level was preserved in AD in comparison to ACDF patients in early (6.9 vs. 0.89 degrees, $p<0.01$, paired student t-test) and late (8.4 vs. 0.53 degrees, $p<0.01$) follow-up. C2-7 ROM was greater in AD patients at late follow-up (53.7 vs. 43.2 degrees, $p<0.04$). ACDF patients demonstrated statistically significant decreases in operative level ROM, translation, and disc height following arthrodesis ($p<0.05$). No significant changes were seen at adjacent levels. *Conclusion:* Adjacent level kinematics were not altered in ACDF patients, despite altered kinematics at the fusion site. AD patients demonstrated greater overall cervical ROM, likely due to retained motion at the operated level.

C-08

Osteogenic protein-1 in high-risk spinal fusion patients: long-term follow-up in 26 patients with independent outcomes-based sssessments

R Perrin (Toronto), P Govender (Toronto), J Furlan (Toronto), Y Petrenko (Toronto), D Salonen (Toronto), S Lewis (Toronto), R Rampersaud (Toronto), E Massicotte (Toronto), M Fehlings (Toronto)*

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Background: Osteogenic protein-1 (OP-1) augments bone formation, and overcomes the adverse effects of nicotine on fusion in animals. However, evidence for efficacy in clinical spine surgery remains unclear. We undertook a prospective study in a high-risk cohort of patients undergoing spinal fusion surgery to evaluate the long-term beneficial effects and safety of OP-1. *Methods:* Patients considered to be at high risk for non-union (e.g. previously failed fusion, heavy smokers, rheumatoid arthritis) were enrolled. Patients were evaluated up to 24 months with SF-36, Oswestry Disability Index (ODI) and dynamic radiographs. At surgery, 3.5 mg of OP-1 with autogenous bone was implanted bilterally. Criteria to assess outcomes included improved survey scores, absence of radiographic instability, and intact instrumentation. Data were analyzed using Student's paired t-test. *Results:* Twenty-six patients were enrolled. Mean follow-up was 11.2 months. The following showed statistically significant improvements post-operatively: ODI scores (p =0.0004), bodily pain (p=0.002), vitality (p=0.038), social functioning (p=0.036), and physical health summary scores (p=0.047) of SF-36. No patient demonstrated radiographic instability. There were no post-operative complications related to OP-1. *Conclusions:* OP-1 was not associated with any complications, achieved successful arthrodesis and significant improvements in outcome scores in this cohort of patients following spinal fusion.

EPILEPSY / EEG

D-01

Linear transform from epileptic spikes to BOLD fMRI signals in an animal model of occipital epilepsy

SM Mirsattari (London), Z Wang (London), JR Ives (London), F Bihari (London), LS Leung (London), R Bartha (London), RS Menon (London)*

Andree Barbeau Memorial Prize winner (See page 6)

D-02

Temporal lobe epilepsy surgery: estimation of resection and correlation with clinical outcome

D. Klironomos (Montreal), N. Bernasconi (Montreal), A. Olivier (Montreal), A. Bernasconi (Montreal)*

Background: Pharmacologically intractable temporal lobe epilepsy (TLE) usually relates to mesial temporal sclerosis. The main structural changes in mesial temporal sclerosis, as determined by magnetic resonance imaging (MRI), include atrophy of the hippocampus, the amygdala and the entorhinal cortex. Surgical removal of the sclerotic mesial temporal structures has proven to be successful in reducing or eliminating seizures in many patients with medically intractable TLE. However, it remains unclear what proportion of the mesial structures is usually removed and to what extent the amount of resection influences surgical outcome. *Methods:* We studied 52 patients with TLE who had high-resolution pre- and post-operative T1-weighted MRI. Volumetric measurements of the hippocampus, amygdala and entorhinal cortex were performed on preoperative MRI in all patients, and showed hippocampal atrophy in 40 patients. 7 patients were excluded who had a long delay between their surgery and their post-op MRI. Patients underwent either a selective amygdalo-hippocampectomy (SelAH; n=33) or cortico-amygdalo-hippocampectomy (CAH; n=12). First, the postoperative MRI was co-registered to the preoperative MRI. Then, the preoperative labels were overlaid on the post-operative MRI and the area corresponding to the resection was deleted from the labels. The amount of resected volume for each structure was determined by calculating the percent difference between the pre- and post-operative labels. Patients were divided in those who were completely seizure free (n=22) and those who were not (n=23). *Results:* In relation to preoperative volumes, patients who achieved complete seizure freedom had smaller hippocampal volumes than those who did not (mean Z -3.77 vs -2.18; p=0.05). Patients who underwent a SelAH had a greater percent resection of the hippocampus than those who underwent CAH (mean 59% vs 37%; p=0.03). On the other hand, patients who underwent CAH had a larger resection of the entorhinal cortex than those who had SelAH (mean 80% vs 54%; p=0.003). In SelAH, patients who became seizure free had a larger resection of the hippocampal body compared to those who did not achieve seizure freedom (mean 46% vs 25%; p=0.048) . In patients who underwent CAH, those who became seizure free tended to have a greater resection of the entorhinal cortex compared to those who did not (mean 90% vs 72%; p=0.22). Patients with residual post-operative auras also tended to have a smaller resection of the hippocampal body (mean 21% vs 39% resected; p=0.14). *Conclusion:* Depending on the type of surgery, the resection of different mesial structures seems to be determinant for achieving seizure freedom.

D-03

A Reappraisal of Rhythmic Coma Patterns in Children

Rajesh RamachandranNair (Toronto), Rohit Sharma (Toronto), Shelly K Weiss (Toronto), Hiroshi Otsubo (Toronto), Miguel A. Cortez (Toronto)*

Background: This study was to determine the prevalence of rhythmic coma patterns, alpha intrusions and reactive EEG patterns in comatose children, to ascertain their prognostic significance. *Methods:* We retrospectively analyzed and classified EEGs in comatose children between 2 months and 18 years of age during the period 1996- 2003 according to modified Young's classification. Outcome at 1-year was scored according to the Paediatric Cerebral and Overall Performance Category Scale (PCOPCS). Outcomes were compared using Fisher's exact test and Mann-Whitney test. *Results:* Analysis of 63 EEG records in 38 patients showed rhythmic patterns in 18 records (28.6%) (9 alpha, 4 spindle, 3 theta and 2 beta coma patterns) and alpha intrusions (alpha frequency occurring less than 50 % of the recording time) in 6. 4 children had a reactive alpha coma (AC) pattern and only 1 had an unfavourable outcome. Reactive pattern did not predict favourable outcome (p=0.16) or lower PCOPCS score (p= 0.056). Outcomes did not differ in AC patterns and alpha intrusions (p= 0.39). *Conclusions:* Rhythmic coma patterns in comatose children are not uncommon. Aetiology, reactivity and outcome of individual patterns are similar and, thus make the rhythmic coma patterns distinct EEG signatures in comatose children. There was a clinically significant better outcome

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with the reactive AC pattern, though only near statistical significance was achieved.

D-04

The role of EEG in the cardiac arrest patients

MS Hussain (Edmonton), PG Brindley (Edmonton), M Jacka (Edmonton), DW Gross (Edmonton)*

Background: Prognostication post-cardiac arrest is difficult, especially when considering non-convulsive status epilepticus (NCSE). While the EEG is the only method of diagnosis, disagreement exists regarding EEG criteria for NCSE, often confusing management. *Methods:* Prospective evaluation of all cardiac arrest patients who had an EEG during admission to intensive care during 2003. Patient outcomes were correlated with EEG findings and clinical factors. Multivariate logistic analysis was performed. *Results:* Of 169 EEGs ordered in ICU, 38 were for cardiac arrest patients. Of these, 3 (7.9%) had definite clinical seizures, 19 (50.0%) had no seizures, and 16 (42.1%) had ambiguous motor activity. Sixteen (42.1%) had no paroxysmal activity on EEG, 5 (13.2%) had periodic epileptiform discharges, 5 (13.2%) had interictal epileptic discharges, and 12 (31.6%) had burst suppression pattern. None had definite electrographic seizures. Thirty-two (84.2%) patients died, 5 (13.2%) were discharged home, and 1 (2.6%) was discharged to long-term care. In multivariate analysis, only low GCS was associated with increased mortality. *Discussion:* While the incidence of paroxysmal EEG patterns was high (57.9%), NCSE was not observed in any patients. Level of consciousness was the most important outcome prognosticator, whereas EEG findings were not. These findings question the overall utility of EEG in cardiac arrest patients.

D-05

Management of status epilepticus in tertiary care emergency room

Taim Muayqil (Edmonton), SN Ahmed (Edmonton)*

Background: According to published literature status epilepticus (SE) is associated with 20% mortality. The time to initiation of treatment and management course potentially have a significant impact on outcome. We sought to audit the sequence of management of SE at the University of Alberta Hospital. *Methods:* We identified 83 encounters of patients 18 years of age or older who presented with SE to our emergency room between 2000 and 2004. 53 met our inclusion criteria. We defined SE as continuous convulsive activity for 5 or more minutes or 2 convulsions without complete recovery in between. Information was collected pertaining to the sequence of management for these patients. *Results:* There were 30 males and 23 females with ages ranging from 18 to 90 years, mean of 45. Sub-therapeutic drug levels were found in the majority 45.3%. Benzodiazepines were the first line agent in 96% mostly initiated by paramedics (EMS).15 patients required intubation and 16 required admission to intensive care. 4 patients died. *Conclusion:* Despite the lack of a standardized treatment protocol among various physicians, benzodiazepines appear to be the favored 1st line agent. EMS plays a major role in immediate management. Analysis of this data will help devise prospective treatment protocols.

D-06

Post-traumatic epilepsy sequel to mild head injuries incurred during recreational hockey games

A Ogunyemi (St. John's)*

Background: The long-term clinical significance of head injuries occurring during hockey games are not fully known. In professional hockey, injuries are documented and treated by health professionals. During recreational hockey games, mild injuries are less likely to be adequately documented or treated. *Method:* Two gentlemen presented with new-onset seizures. Both of them had neurological assessment and regular follow-up at the Seizure Clinic, St. John's NL. The clinical assessment included detailed clinical history, physical examination, blood tests, neuroimaging studies and EEG recordings *Results:* For both men, the general and neurological examinations and all the relevant blood tests were normal. For the 45-year-old man (DA), multiple EEG recordings, CT brain and the MRI brain were normal. However, a repeat MRI brain, performed 12 years after the initial one, was abnormal, showing signs of remote contusion involving the orbitofrontal cortex For the 65-year-old man (HS), the EEG showed focal delta waves and epileptiform potentials in the left frontotemporal region. His MRI brain revealed signs of old bilateral orbitofrontal and right temporal pole contusion. Following the positive MRI findings, both men recalled having sustained mild head injuries during recreational hockey games, when they were 17 and 20 years old, respectively. Neither man was hospitalized at the time of the injury Their epileptic seizures were controlled with antiepileptic drug monotherapy *Conclusion:* Late-onset epilepsy may be an aftermath of relatively mild head injury incurred during recreational hockey games. MRI brain with special attention to the orbitofrontal surface of the brain may provide the diagnostic solution.

D-07

Levetiracetam: A clinical audit in two Canadian adult epilepsy clinics

N Pillay (Calgary), A Guberman (Ottawa)*

Background: Levetiracetam (LEV) was released in Canada as adjunctive therapy in the management of patients with epilepsy who are not satisfactorily controlled by conventional therapy, in July 2003. It has a novel mechanism of action, favorable pharmacokinetics without drug interactions, and no serious adverse effects. Responder rates (e50% seizure reduction) in 3 pivotal randomized, controlled trials were 35-40% at doses of 2 to 3 g/day We analyzed all cases started on LEV from adult epilepsy clinics in Calgary (N=86) and Ottawa (N=35) prior to November, 2004. *Methods:* Retention, duration of treatment, reasons for discontinuation, titration schedules and maintenance doses, concurrent therapy and response were analyzed. *Results:* Sixty-four males and 57 females, mean age 36.6 years, 108/121 with partial or secondarily generalized seizures and 13/121 with primary generalized epilepsy, were treated. Seven were converted to monotherapy on LEV and the remaining (114) were on polytherapy and majority (89) of the latter were on 1 or 2 AEDs. Continuing patients were followed for a mean of 6.5 months (62/120 e6 months). Titration was slow (d500mg/day/week) in 50/121 and

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e500mg b.i.d. in 70/121. LEV was discontinued in 41/121 (33.8%), due to side effects (mostly minor). Seizures increased in 6/120 (0.05%). Psychiatric adverse effects (PAE) occurred in 27/121 (22.3%). Discontinuations occurred in 17/27 with PAE and 10/27 continued despite PAE because of better than 50% seizure improvement. Psychosis emerged in 3/121 (2%). All side effects, including PAE, reversed promptly on discontinuation of LEV. Efficacy was judged as good or better in 63/120 (52.5%), and 20/120 (16.7%) were seizure-free. *Conclusions:* 1. Levetiracetam as an add-on AED in localization-related epilepsy has favorable efficacy in clinical use. 2. Psychiatric adverse effects are more common than reported in controlled trials but reverse rapidly on withdrawal of levetiracetam. 3. Discontinuations due to adverse effects did not appear to be related to dose or the speed of titration.

D-08

Scalp electrodes for long term EEG monitoring in ICU

B Young (London), J Ives (London), S Mirsattari (London), Chapman M (Toronto)*

Background: The reliability of long-term EEG monitoring (LTM) primarily depends on the integrity of the scalp electrodes. *Methods:* We studied the simultaneous use of subdermal wire scalp electrodes (SWE) and standard, collodion-applied disk electrodes (CADE) for LTM of 10 patients in the neuro-ICU. Records were read without knowledge of which electrode system was being used. *Results:* CADE began to fail between 3-6 hours in a characteristic manner: 60 Hz artifact, then low voltage rhythmic waves followed by high voltage artifact at various frequencies. No scalp electrode position was more likely than others to fail. In contrast, SWE remained stable thought the 24-48 hour recordings. *Conclusion:* CADE fail in a characteristic manner with LTM, beginning after 3 hours. No site is more likely than others to fail. This information has potential usefulness for interpretation and constructing alarm systems for LTM. SWE provide stable recordings for 24-48 hours.

Pediatric Neurology / Neurosurgery

E-01

The use of ventriculosubgaleal shunts in the treatment of hydrocephalus in premature infants. G Marchuk* (Winnipeg, Manitoba), P McDonald (Winnipeg Manitoba)

Graeme Marchuk (Winnipeg), Patrick McDonald (Winnipeg)*

Background: Ventriculosubgaleal shunts (VSGS) have recently been advocated as a means of temporarily bypassing normal CSF pathways when conditions are not favourable for permanent shunting. Experience with their use in Canada has not been extensively reported. *Methods:* A retrospective chart review of all ventriculosubgaleal shunts at Winnipeg Childrens Hospital was undertaken. Demographic data, indications for shunting, shunt life, mode of failure and clinical outcomes were assessed. *Results:* There were eight cases of VSGS insertion during the period 2003 - present. The indication in all cases was posthemorrhagic hydrocephalus related to prematurity and all children weighed less than 2000g at the time of VSGS insertion. Average shunt life was 34 days (range: 16-68 days). The cause of shunt failure was shunt obstruction in 3 and eventual impairment of CSF absorption by the scalp in 5. There were no complications related to ventriculosubgaleal shunting. All children went on to have a permanent ventriculoperitoneal shunt placed when conditions were more favourable. *Conclusions:* Ventriculosubgaleal shunting remains a safe, and technically simple alternative to other means of temporary CSF diversion, and a useful means of temporizing hydrocephalus prior to definitive CSF shunting.

E-02

Perinatal factors associated with the development of childhood epilepsy: A population-based cohort study

J Dooley (Halifax), L Dodds (Halifax), E Whitehead (Halifax), KS Joseph (Halifax), K Gordon (Halifax), E Wood (Halifax), A Allen (Halifax)*

Objective: To identify and examine the contribution of perinatal factors in the development of childhood epilepsy. *Methods:* A population-based cohort was assembled through record linkage of two population-based databases; the Nova Scotia Atlee Perinatal Database and the Canadian Epilepsy Database and Registry (CEDaR). Children born between January 1986 and December 2001 in Nova Scotia were followed to December 2001. Perinatal factors significantly associated with the development of epilepsy were identified from proportional hazard models. Population attributable risks and predictive probabilities were determined using this set of factors. *Results:* There were 124,207 births during the study period and 648 cases with epilepsy. This analysis included 110,130 who had no missing data on the risk factors; 564 children developed epilepsy (overall risk 0.56%). Only prenatal and neonatal factors were significantly associated with epilepsy. Factors included neonatal seizures, CNS and non-CNS anomalies, CNS disease and neonatal metabolic disorders. An increased risk was also associated with: eclampsia, abruptio placenta, previous low birth weight infant, small for gestational age and infection in pregnancy. The population attributable risk for the 10 significant factors was 27.8%. A scoring system was developed to predict the risk of epilepsy. *Conclusions:* This study shows an association between epilepsy and perinatal risk factors with almost 30% of seizures attributable to 10 identified factors. A scoring system allows prediction of the risk of epilepsy.

E-03

Apparent diffusion coefficient (ADC) maps may predict neurodevelopmental outcome following perinatal hypoxic-ischaemic encephalopathy (HIE) in term infants

S Levin (London), J Winter (London), D Lee (London), R Hung (London), N Gelman (London), T Thompson (London)*

Background: There are no data on the reliability of ADC maps to predict outcome in term infants sustaining perinatal HIE. *Methods:* Twelve term infants diagnosed with intrapartum HIE had magnetic resonance imaging scans performed in the first 20 days of life with ADC maps generated from diffusion-weighted images. Four patients had two scans. *Results:* ADC values obtained from the posterior limb of the internal capsule, lentiform nucleus and thalamus all produced significant regressions with respect to postnatal age when

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compared with neurodevelopmental outcome. For these brain regions, ADC values less than 1.0x 10-3 mm^2/s or greater than1.25x10-3mm^2/s at any time predicted poor outcome. Patients with ADC values within the normal range had a normal outcome. Results from brainstem and cerebellum were not significant. In cases with serial scans ADC values changed from abnormally low to normal to abnormally high values with increasing age. *Conclusions:* This pilot study suggests that ADC maps predict outcome with a high degree of accuracy. One reason for false negative results with DWI and ADC may be that the imaging is done in the period of false normalization of the data. Our data suggest that a second scan done 5-7 days after the first scan would eliminate this error.

E-04

Acute severe encephalopathy in diabetic ketoacidosis: a 10 year retrospective review

C Waisburg (Vancouver), S Basheer (Vancouver), G Hendson (Vancouver), M Sargent (Vancouver), M Bennet (Vancouver), D Metzger (Vancouver), J Hukin (Vancouver)*

Background: Around 7/1000 episodes of childhood DKA are complicated by cerebral edema (CE/DKA). Death is reported in 90% of cases of childhood CE/DKA. The objective of this study is to examine the biochemical, clinical, neuroradiological and neuropathological findings of children with CE/DKA, to identify factors associated with this condition. *Methods:* Children, identified from our neuroradiological database (1994 - 2004), transferred to BC Children's Hospital ICU with acute severe / progressive encephalopathy and DKA were selected. A retrospective review of clinical records, neuroimaging, biochemical profiles, and pathological findings was performed. *Results:* Six patients were identified, five had associated cerebral herniation and four died. The mean time to brainstem herniation was 6.5 hrs (4.5-9.5 hrs). Neuroimaging and pathology revealed diffuse cerebral edema and ischemic changes of basal ganglia, brainstem, posterior circulation and internal capsule. All patients had rates of change of corrected Na >10mmol / 24hr and glucose correction >1.5mmol / hr up to the time of herniation. *Conclusion:* CE/DKA is of rapid onset, occurring within the first 12hrs of resuscitation. Despite strict therapeutic guidelines, CE/DKA may occur. This study demonstrated that first presentation and progressive decline in sodium with neurologic change are risk factors for CE/DKA.

E-05

Is it possible to predict the outcome of Shaken Baby Syndrome?

K Barlow (Calgary), B Vanmastrigt (Calgary), A Ells (Calgary), L Hogan (Calgary), N Ho (Calgary)*

Introduction: The outcome of Shaken Baby Syndrome (SBS) is generally poor with less than 25% of children being normal on long-term follow-up and the level of disability varies from mild to severe. If it was possible to predict the outcome it might be possible to target available resources more efficiently. *Methods:* Part 1: Cross-sectional study. Several variables during the acute admission were analysed including the Pediatric Trauma Score (PTS), presence of Early Post-traumatic Seizures (EPTS) and cerebral oedema (CO) on neuroimaging within the first 72 hours of admission. Outcome measure: Seshia's outcome score. Multiple linear regression analysis was used to provide a fitted model equation to estimate outcome. Part 2: Subsequent cohort of children with SBS and accidental traumatic brain injury as infants. The examiner was blinded to the mechanism of injury. The outcome was predicted using PTS, EPTS and CO. A comparison was made between the actual versus the predicted outcome using the Fitted Model. *Results:* 18 children with accidental (4) and inflicted (14) were analysed. The outcome was successfully predicted in 15 out of 18 children. The correlation coefficient was +0.72 ($p < 0.05$). *Conclusions:* It was possible to predict the outcome of Shaken Baby Syndrome in this small sample. It remains difficult to recruit and monitor the progress of children with Shaken Baby Syndrome due to the complex medicolegal and social circumstances that exist in this group of children.

E-06

Canadian Survey of Surgery for Intractable Epilepsy in Children

W Hader (Calgary), P Steinbok (Vancouver), B Sinclair (Edmonton), J Rutka (Toronto), E Ventureyra (Ottawa), M Vassilyadi (Ottawa), J Montes (Monteal), JP Farmer (Montreal), P Mcdonald (Winnipeg), R Griebel (Saskatoon)*

Background: Rationale for the greater use of surgery for the treatment of temporal lobe epilepsy in children has previously been proposed. In addition, surgery for TLE in adults, most of whom developed epilepsy in childhood, has been shown to be superior to prolonged medical therapy in a randomized controlled trial. The purpose of this study was to assess the impact of the support for temporal lobe surgery, on the number of procedures being performed for intractable epilepsy in children. *Methods:* A single page survey was emailed to all neurosurgical centres in Canada known to perform surgical treatment for intractable epilepsy in children. All procedures performed over a one year period were recorded. *Results:* Nine centres responded to the survey. The total number of cases of all surgical treatments performed for intractable epilepsy in children was 165. Thirty-one (19%) patients underwent temporal lobectomies, 60 (36%) patients either a lesionectomy or cortical resection and 30 (18 %) patients underwent palliative procedures. Twenty five (15%) patients underwent invasive monitoring prior to definitive surgical resection. *Conclusions:* Traditional temporal lobe surgery for the treatment of refractory epilepsy in children is performed no more frequently than lesionectomy, cortical resections or palliative procedures. The exact reason for the low rate of termporal lobe surgery in children is unclear.

Stroke / Pediatric Stoke

F-01

Cerebral venous sinus thrombosis: early combined angioplasty and endovascular thrombolysis ensures better outcome

C Sivakumar (Calgary), S Subramaniam (Calgary), J Roy (Calgary), JM Boulanger (Calgary), V Palumbo (Calgary), MD Hill (Calgary), W Hu (Calgary), T Watson (Calgary)*

Background: Despite the belief that cerebral venous sinus

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thrombosis (CVST) has very good outcome in terms of functional independence, 22-44% have mild to moderate impairment. Hence the need for newer therapies to ensure patency and better long term outcomes. Prospective identification of those patients at greatest risk for permanent morbidity and mortality is difficult, hence individualised treatment is still the case. *Method:* We report a 32 year old female patient with superior sagittal sinus (SSS) and transverse sinus (TS) thrombosis presenting acutely with worsening headache, drowsiness, papilledema and at risk of neurological deterioration as evidenced by angiographic findings. She was successfully treated by early combined endovascular thrombolysis and angioplasty. *Results:* Follow up at three months showed no neurological sequele. Repeat MRI showed complete filling of all sinuses with no evidence of parenchymal damage. *Conclusion:* In specialist centers, for a select group of high risk patients, combined endovascular thrombolysis and angioplasty of SSS and TS thrombosis may be tried as a first-line therapy for rapid flow restoration, clinical improvement, long term venous patency and even better outcome in CVST.

F-02

Awareness of warning symptoms of stroke and heart disease - A pilot study of the Chinese Canadian cardiovascular health project

JY Chu (Toronto), CM Chow (Toronto), GW Moe (Toronto), J V Tu (Toronto)*

Background: Chinese is one of the largest visible minority in North America. Chinese account for 27.5 of all visible minority groups in Canada . Moreover, a substantial portion of the North American Chinese population are recent immigrants. Their knowledge in stroke, heart disease and health beliefs have not been well established. Information of the cardiovascular health of this population is therefore of importance to the allocation of health care and promotion resources. In this pilot study, we sought to define the awareness of the warning signs and risk factors for stroke and heart disease in the Chinese Canadian population. *Methods:* A random 16-item telephone survey was conducted among 1,004 ethnic Chinese (>=18 years old) in Greater Toronto (N=503) and Vancouver (N=501) in Feb., 2004. The parameters that were obtained included knowledge for heart disease and stroke such as signs and symptoms for stroke, acute myocardial infarction (AMI), health habits, and initial response in case of a cardiovascular emergency. *Results:* 58% of the respondents were females while 62% were under 45 years old. 71% speak Cantonese at home and 21% speaks Mandarin. 97% were immigrants with 53% being in Canada for less than 10 years. 9.2% reported to have history of hypertension, 3.2% has diabetes and 17.5% with high cholesterol. Ability to correctly identify stroke and AMI symptoms (unaided): STROKE AMI Unable to name at 40% 32% least one symptom At least one incorrect 35% 32% symptom named. There was no gender or age difference in the ability to name symptoms of stroke or AMI. Respondents who lived in Canada more than 10 years were less likely to name at least one AMI symptoms(OR 0.76, 95% CI = 0.58-0.99, p=0.04). When asked about the initial response in case of AMI or stroke, only 20% will call 911. Only 48% of the respondents exercise at least 20 minutes 3 times a week. *Conclusions:* This is first study targeted at North American Chinese regarding their knowledge of stroke and heart disease. These data suggests that Chinese Canadians have relatively low awareness of warning signs for common stroke and heart attack symptoms. Our findings have important implications in the development of future health promotion initiatives targeted to this large mainly immigrant population to address specific knowledge gaps and misconceptions in stroke and heart disease, and warrant further large-scale studies.

F-03

Intracranial giant cell vasculitis with cerebral amyloid angiopathy: an unusual combination.

J Diggle (Calgary), K Heathcote (Saskatoon), N Pillay (Calgary)*

Background: Giant cell vasculitis of the central nervous system (CNS) is a rare disease process involving inflammation of small-to-medium sized leptomeningeal and intracranial vessels in a focal and segmental distribution. CNS vasculitis can be classified as a primary disease process (primary CNS vasculitis) or as secondary to a systemic disorder. Recognition of secondary causes can have a significant impact on the investigation, treatment, and prognosis in these patients. In the literature, there are only rare case reports of CNS vasculitis being associated with a cerebral amyloid angiopathy (CAA). The vasculitis seen in the setting of CAA most likely represents a foreign body response to amyloid proteins, causing secondary destruction of the vessel wall. We would like to report a case of CAA associated with pathologically-defined giant cell vasculitis of the nervous system. *Methods:* A 68-year-old woman with a history of mitral valve prolapse and hypothyroidism presented to the emergency department with a generalized tonic-clonic seizure after a four week history of clumsiness, unsteadiness, and a retro-orbital/temporal headache. Examination demonstrated a left homonymous hemianopsia. Astereognosis and graphesthesia was found on the left. She was unable to perform tandem gait. *Results:* Serial magnetic resonance imaging (MRI) of the brain showed progressive dural and leptomeningeal enhancement over the right hemisphere with increased T2 signal in the right parieto-occipital cortex. Electroencephalography (EEG) showed right posterior temporal sharp waves and right hemispheric slowing. Lumbar puncture and catheter angiography of the brain were normal. A diagnosis of angiitis of the central nervous system was made after open biopsy of the dura, leptomeninges, and cortex. The vasculitic change was associated with a pronounced underlying cerebral amyloid angiopathy. Work-up for systemic amyloid was unremarkable. The patient was started on 75 mg prednisone daily, and was discharged home once her symptoms began to improve. *Conclusion:* Though diagnostically challenging, progressive leptomeningeal disease with cortical change should prompt consideration of CNS vasculitis. In the setting of normal catheter angiography and lumbar puncture, open leptomeningeal and brain biopsy is warranted to support the diagnosis. Once confirmed pathologically, the recognition of secondary causes of CNS vasculitis can have important implications for patient care. Small and medium vessel giant cell arteritis is uncommon and the association with amyloid angiopathy is unusual.

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F-04

Headache and migraine in children with stroke

Melissa Martin (Toronto), Trish Domi (Toronto), Mubeen Rafay (Toronto), Marianne Sofronas (Toronto), Kristy McCurdy (Toronto), Ross Curtis (Toronto), Gabrielle deVeber (Toronto), MacGregor Daune (Toronto)*

Background: A causal relationship between migraine and stroke is debated; pediatric literature lacks data on characteristics of headache in stroke population. *Objective:* Determine the prevalence of migraine and headache in children, before and after stroke. *Methods:* Children with arterial ischemic stroke(AIS) and cerebral sinovenous thrombosis(CSVT), at Hospital for Sick Children, from January1995-December2003. Data was collected using the Pediatric stroke outcome measure(PSOM) and headache questionnaire incorporating the international headache society criteria. *Results:* 205 children were identified with AIS(79%), CSVT(19%), and both(2%), median-age at stroke 3.3-year. 71(35%) children reported headache(52%migraine). At 5-year follow-up, 32%had migraine, whereas migraines occur in 4-5%of school-aged children(p 0.0001). 21(30%) children, aged 5-year, reported headache before stroke(67%migrainous), 58(28%) following stroke, with prior headache in 15(73%migrainous) and without prior headache in 43(44%migrainous). Following differences were identified between headache and non-headache patients: vasculopathy(p 0.003), family history of migraine(p 0.009), head and neck trauma(p 0.009) and connective tissue disorder(p 0.013). Gender, stroke-type, prior headache and vascular territory did not reach significance. *Conclusion:* Post stroke migraine was significantly higher compared to the incidence of migraine in children. We have identified some consistent predictors of headache following stroke. Considering trigeminovascular theory of migraine, we hypothesize that cranial vessel wall involvement leading to stroke may sensitize or activate these pathways.

F-05

Intrauterine bilateral middle cerebral artery stroke secondary to inferior vena cava thrombosis: A case report

A Attar (London), S Levin (London)*

Background: Neonatal strokes are rare, with a frequency of 1 in 10 000. The underlying cause for these strokes is not always known. Neonatal portal vein thrombosis has been reported as causing middle cerebral artery (MCA) territory strokes. *Methods:* Case report of an intrauterine, bilateral, MCA territory stroke secondary to idiopathic inferior vena cava (IVC) thrombosis. *Results:* The patient was a full term male delivered as uncomplicated spontaneous vaginal vertex delivery to a healthy 27-year-old, gravida 2, para 0, mother. Birth weight was 4160 grams. Apgar scores were 5, 8 and 9 at 1, 5 and 10 minutes respectively. He required bagging and suction for a short time. The baby was "jittery" from birth but had normal medical and neurological examination. Few hours after birth, the baby was noted to have lip smacking and bicycling movements. Blood gases, pH, electrolytes, glucose, CBC and cerebrospinal fluid analysis were within normal limits. He was treated initially with dilantin and ampicillin and gentamicin pending septic work-up results. Initial EEG showed frequent seizures, apparently originating sagitally and spreading to the right posterior-temporal-occipital regions. Brain MRI findings were consistent with recent, massive right MCA territory infarction and a well-established old infarct of the left MCA territory. Two-dimensional echocardiogram showed evidence of IVC thrombosis. Thrombophilia studies were negative. *Conclusion:* We hypothesize that the bilateral MCA territory infarcts were caused by emboli from the IVC thrombosis, a pathophysiologic event not previously reported.

F-06

Predictive value of seizure and EEG features of neonatal stroke and hypoxic ischemic encephalopathy

Mubeen Rafay (Toronto), Cherrie Tandy (Victoria), Amna Al-Futaisi (Muscat), Woojin Yoon (Toronto), Aideen Moore (Toronto), Miguel Cortez (Toronto), Gabrielle deVeber (Toronto)*

Background: Both hypoxic ischemic encephalopathy (HIE) and stroke present with neonatal seizures. Since neonates often have non-localizing examination, clinical and electroencephalographic (EEG) features may provide means of early diagnostic differentiation. *Objectives:* To compare and predict seizure and EEG features of neonatal stroke and HIE. *Methods:* Neonates, 36-weeks gestation or more, with seizures within 7-days after birth and diagnosis of HIE or stroke, seen at Hospital for Sick Children, from January 1992-September 2003. *Results:* Seventy gestational age-matched newborns, with seizures (35 stroke and 35 HIE) were identified. With univariate analysis, significant differences were identified with the following: mean time of seizure onset from birth (34.7 hours in stroke versus 5 hours in HIE, p less than 0.001, with seizure onset within 24 hours in all HIE neonates), focal seizures (p 0.001), abnormal background (15 stroke versus 23 HIE, p 0.05), lateralized EEG findings (p 0.04), midline EEG findings (p 0.01), and response to antiepileptic therapy (p 0.025). With multivariate analysis, seizure onset (p 0.002), focal seizures (p 0.045) and background type (p 0.02) reliably predicted stroke. *Conclusion:* Our findings suggest that, seizure onset 24 hours after birth, focal seizures and background reliably predict stroke in newborns with seizures. These predictors support appropriate neuroimaging for timely diagnosis of neonatal stroke.

General Neurosurgery

G-01

Preserved hearing after intraoperative loss of the brainstem auditory evoked potential during vestibular schwannoma surgery

R Yong (Vancouver), R Akagami (Vancouver)*

Background: Brainstem auditory evoked potentials (BAEPs) are used in vestibular schwannoma surgery to monitor the function of the cochlear nerve and the brainstem auditory pathways. Wave III arises from the region of the superior olivary complex while wave V reflects activity in the inferior colliculus. Intraoperative loss of these waves with preservation of wave I is believed to correlate with poor postoperative hearing, although false-positive changes can occur. *Methods:* A consecutive series of 37 patients with vestibular

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schwannomas underwent microsurgical resection with intraoperative BAEP monitoring. The series was retrospectively examined to determine the rate of intraoperative wave III and wave V loss, and to compare this with the rate of hearing preservation. *Results:* Seventeen of 37 patients had complete loss of waves III and V. Of these, 3 patients had long-term serviceable hearing postoperatively, defined as a speech reception threshold of less than 50 dB and a speech discrimination score of at least 50% at 6 weeks or later. *Conclusions:* Intraoperative loss of waves III and V with serviceable hearing postoperatively may be more common than previously thought. Subclinical changes in the BAEP may be due to the development of asynchronous conduction within the cochlear nerve as a result of tumour dissection.

G-02

Jobs wanted: Patriotic academic neurosurgeons for hire

S Woodrow (Toronto), C O'Kelly (Toronto), S Hamstra (Toronto), C Wallace (Toronto)*

Background: There is growing concern about limited employment prospects for neurosurgical residents in Canada. The purpose of this study was to investigate the perception of current trainees regarding their future career goals and employment prospects. *Methods:* In the spring of 2004 all Canadian neurosurgical residents were invited to complete an internet-based survey. The questionnaire consisted of short answer questions and questions formatted on a 5-point Likert scale. *Results:* Seventy eight percent (80/102) of residents completed the survey. Eighty percent (64/80) of residents expected to have graduate degrees upon completion of their residency with the majority (62/80) intending to do research as part of their future practice. Almost all (76/80) planned on additional fellowship training, most commonly in cerebrovascular and spine surgery. The vast majority (72/80) of residents wished to practice in Canada and were cautiously optimistic about the potential to do so. The limitation on employment opportunities in the United States was well appreciated by younger trainees. *Conclusions:* The results suggest that we are training neurosurgery residents with a strong academic focus who wish to remain in Canada to practice. We question whether there is room in the current neurosurgical workforce - both in number and scope - to accommodate them appropriately.

G-03

Neurolept versus general anesthesia for the treatment of chronic subdural hematoma

B Jhawar (Toronto), O Hayani (Toronto), J Barbero (Toronto), M Cusimano (Toronto)*

Introduction: The purpose of this study was to determine whether neurolept (NLPT) analgesia is safer than general anesthesia (GA) for preventing complications following burr-hole drainage of chronic subdural hematoma (CSDH). *Methods:* The medical records and operative reports of all patients treated surgically for CSDH at St. Michael's Hospital (Toronto) between 1999 and 2002 were reviewed. Logistic regression models were constructed to predict death, major complications and repeat operation. *Results:* Burr-hole drainage was used to treat 386 patients (n=75 were bilateral). NLPT required less operative time (NLPT=1.03 hours; GA=1.31 hours). More deaths occurred in the GA group (GA=8.3%; NLPT=6.4%), but this was not statistically significant (p=0.56). In multivariate analysis, GA patients were 1.61 (95% CI=0.71-3.86) times more likely to die than those who received NLPT. There were more major complications in the GA group (p=0.02; GA=22.1% and NLPT=13.3%) and this remained statistically significant in multivariate analysis (OR=2.41; 95% CI=1.32-4.39). Anesthetic type did not predict repeat operation (p=0.72). *Conclusion:* For the treatment of patients with CSDH we found that neurolept analgesia required fewer OR resources and was less likely to result in major complication. Neurolept may also improve survival, but we did not have the statistical power to determine this.

G-04

Anticonvulsant prophylaxis for seizure-free patients with newly diagnosed brain tumours: A meta-analysis

L Crevier (Hamilton), R Lai (Hamilton)*

Background: The reported incidence of seizures varies from 20 to 40% in patients with primary or metastatic tumours. The use of anticonvulsants to prevent an initial seizure in this patient population remains controversial. *Methods:* We conducted a systematic quantitative overview of the randomized trials addressing this issue. The search included MEDLINE (1966-February 2004), EMBASE, and The Cochrane Library. The data analysis was performed with RevMan 4.2 (The Cochrane Collaboration). The effect size estimates of each study were combined, after significant heterogeneity had been ruled out ($p > 0.05$), to estimate the overall effect size across studies and 95% confidence intervals were calculated around the point estimate. A priori hypotheses regarding sources of heterogeneity were explored. *Results:* Only 4 of the 74 trials identified met the eligibility criteria for the overview. The overall pooled odds ratio failed to demonstrate a benefit of anticonvulsant prophylaxis. The limitations of this study were discussed. *Conclusions:* Although this study suggests no benefit of anticonvulsants, we believe that this important issue remains unanswered by the current best evidence available. A well designed randomized trial is required to elucidate the true effects of seizure prophylaxis in the brain tumour population.

G-05

Progression of traumatic cerebral contusions: prevalence and risk factors

S Griffith MD (San Antonio), JL Caron MD FRCSC FACS (San Antonio), D Jimenez MD FACS (San Antonio)*

Background: The incidence of progression of brain contusions is not well known. We hypothesize that cerebral contusions evolve rapidly. Goal of this observational cohort study is to identify a population subset most likely to benefit from intervention. Study will also provide preliminary data for power and sample size calculations for further prospective randomized trials on hemorrhagic brain contusions. *Method:* Observational cohort study to identify the following parameters: 1) Prevalence in the moderate and severe TBI population. 2) Incidence of progression on sequential CT scanning. 3) Time line for progression. 4) Identify risk factors associated with progression. 5) Identify sub-groups at risk. 6

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months data from the UTHSCSA Trauma Registry TBI GCS< 12 and 2 CT within the first 24 hours. *Results:* 38 (16.2%) out of 235 had documented brain contusions on initial CT. 10 children (26%) 28 adults (74%); 33 (87%) cortical, 3 (8%) subcortical, 2 (5%) cerebellar. Average interval between scans =13.8 hours. Progression in 29 (76.3%) =5/10 (50%) pediatric, 23/28 (82.1%) adult, 24/33 (73%) cortical, 3/3 (100%) subcortical, 2/2 (100%) cerebellar. Subcortical contusion volume increased x 3, cortical x 2. *Conclusions:* Progression of traumatic brain contusions is more frequent then previously described. A therapeutic window therefore exists for potential preventive measures.

G-06

Characterization of HIF-1alpha/VEGF in human astrocytoma progression

*B Lo** (Hamilton), H Aljawad (Hamilton), K Reddy (Hamilton), R Hollenberg (Hamilton), J Provias (Hamilton)*

Background: Brain tumour growth and progression is supported by angiogenesis. Hypoxia occurs if the tumour rapidly outgrows its blood supply. In order to adapt to hypoxic conditions, it produces angiogenic mediators, including vascular endothelial growth factor and the newly-identified hypoxia-inducible factor-1alpha. In this project, HIF-1alpha and VEGF are characterized as markers for detection of astrocytoma progression. *Methods:* 30 cases of astrocytomas (10 cases each, low, intermediate and high grade) were randomly selected (1999-2004). Immunohistochemistry was performed with anti-HIF-1alpha and anti-VEGF antibodies (dilution 1:50). The labelled strepavidin-biotin-peroxidase complex technique was used for visualization. Positive control: colon carcinoma, negative control: non-diseased autopsy brains. *Results:* Immunohistochemical staining shows: (1) increasing staining intensity for HIF-1alpha/VEGF with increasing proportion of stained cells in increasing grades of astrocytomas, (2) at a particular grade, staining for HIF-1alpha is stronger than that of VEGF, and (3) HIF-1alpha/VEGF expression occurs in tumour core and periphery. *Conclusions:* (1) Level of HIF-1alpha/VEGF expression is increased with increasing grades of astrocytomas, (2) HIF-1alpha is expressed before that of VEGF, and (3) HIF-1alpha/VEGF are expressed in both tumour core and periphery, indicating likelihood of angiogenesis and tumour spread, even before histological and radiological changes are detected. Thus, the clinician can refine the extent of surgical resection in an attempt to delay tumour progression and recurrence.

General Neurosurgery

H-01

Neurovascular Compression Findings in Hemifacial Spasm

M Campos Benitez (Winnipeg), A Kaufmann (Winnipeg)*

Background: Neurovascular compression (NVC) of the facial nerve root entry zone (REZ) has been postulated as the etiology of hemifacial spasm (HFS). We assessed the anatomic classification of culprit NVC seen during microvascular decompression (MVD) surgery. *Methods:* A consecutive series of 115 HFS patients that underwent MVD surgery was analyzed. The location of NVC was categorized as follows: R1=pontomedullary sulcus origin; R2=pontine surface; R3=detachment; R4=distal facial nerve root. *Results:* The senior author performed 115 MVD procedures for patients with HFS, between 1996 and 2004. Culprit NVC was found in all cases, and in descending order of frequency was attributed to the AICA; PICA; vertebral artery; and large vein, at the R2; R3; R1; and R4 portions of the facial nerve root. R4 compression, found in two cases, caused severe nerve distortion. Intraoperative recordings of abnormal electrophysiological response (i.e. lateral spread) was successfully abolished or reduced in over 90%, while complete spasm elimination was achieved in 84%, and spasm relief in another 7%. *Conclusions:* NVC was consistently found and successfully alleviated during MVD surgery for HFS. The varied NVC findings suggest that location of compression upon the facial REZ or distal root may be more related to gross anatomical configuration rather than physiological properties of transitional zone between central and peripheral myelin

H-02

Facial motor evoked potentials during microvascular decompression (MVD) for hemifacial spasm (HFS): New evidence for a hyperexcitable VII nucleus.

M Wilkinson (Winnipeg), A Kaufmann (Winnipeg)*

Background: Lateral spread (LS) is the characteristic EMG signature of HFS and may be due to enhanced motor neuron excitability within facial nucleus. We speculated that if the facial nucleus is hyper-excitable in HFS we should see evidence of this using facial motor evoked potentials (fMEP). *Methods:* LS and bilateral fMEP monitoring were performed on 8 consecutive patients using needle EMG techniques during MVD for HFS. fMEP were achieved using single anodal pulses at C3 and C4. fMEP latency, amplitude and duration were compared between the spasm side, the non-symptomatic side as well as 7 control patients undergoing monitoring during MVD for Trigeminal Neuralgia. *Results:* Following MVD LS was abolished. Baseline fMEP had significantly elevated duration and amplitude versus the non-spasm side. With MVD, HFS fMEP duration decreased from 18.1 ± 1.2 ms to 7.7 ± 0.7 ms and amplitude from 246.7 ± 70.4 _V to 66.8 ± 27.5 _V ($p < 0.03$). These changes were consequent to the elimination of LS in 7 of 8 patients and 50% reduction in one. The duration and amplitude of fMEPs from the asymptomatic side were 12.5 ± 2.3 ms and 179.8 ± 95 _V respectively, which did not change significantly during the MVD procedure. The fMEP latency were similar and stable, bilaterally during MVD for HFS and TN. All patients were alleviated of the HFS postoperatively. *Conclusions:* This study is the first to investigate the neurophysiology of HFS using fMEP in conjunction with LS monitoring. The enhanced characteristics of ipsilateral fMEP and the subsequent reduction of this response closely follows the changes seen in LS during the MVD procedure. The data support the hypothesis that the facial motor neuron excitability is involved in the mechanism explaining HFS.

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H-03

Monitoring Pain level and Clinical Outcomes in the Treatment of Trigeminal Neuralgia

A Kaufmann (Winnipeg)*

Introduction: The purpose of the study is to evaluate patients perceived pain level and treatment satisfaction for trigeminal neuralgia (TN) using a new automated data collection, analysis and reporting system. *Methods:* An instruction sheet was mailed to a subset of patients with facial pain, registered at our Centre for Cranial Nerve Disorders to call a toll-free number and respond to the automated system. Two questionnaires were used: TN management questionnaire (TNMQ) and McGill pain questionnaire (MPQ). *Results:* Among the 156 respondents, the mean age was 63 years, 59% were females and 65% had typical TN. The questionnaires were completed in 6.4 and 4.6 minutes for the TNMQ and MPQ, respectively. 58% of patients reported having at least one rhizotomy, 56% had at least one microvascular decompression, and 43% were currently taking pain medication. Patients treated for typical TN reported lower pain levels and higher satisfaction compared to those with atypical TN and other types of facial pain ($P < 0.05$). There was strong inverse correlation ($r = -0.7$) between MPQ pain rating indices and TNMQ-reported patient satisfaction ($P < 0.0001$). *Conclusion:* The proposed system provides an innovative method to monitor pain status and treatment outcomes in patients with facial pain. This system is further being evaluated to provide monthly follow-up assessments and may be applied to a broad range of clinical and research uses.

H-04

Experimental Image-guided Trans-sphenoidal Endoscopic Pituitary Surgery : A Useful Learning Set-up.

Jian Gong (Montreal), Gérard Mohr (Montreal), Jean Vézina (Montreal)*

Background: In order to assess the potential impact of image guidance in endoscopic pituitary surgery, we elected to revisit the surgical anatomy of the sphenoid sinus and sella turcica under experimental endoscopic conditions and to analyze quantitatively the additional stereo-information provided by an electro-magnetic field neuronavigation-system in terms of reliability and accuracy. *Methods:* Using global CT-scannning with fiducial landmarks, ten adult cadaveric heads were studied with 0-, 30-, and 70-degree endoscopes (4-mm rod-lens, Karl Storz) under simultaneous image guidance (InstaTrack GE). The sphenoid sinus was exposed via endonasal paraseptal approach and anatomical structures of the sellar region, anterior fossa, cavernous sinus and clivus were recorded systematically. The accuracy of the neuronavigation system was tested using millimetric optical verification and anatomical variations were documented, measured and photographed. *Results:* A reference database with optic - radiologic correlations of most important topographic landmarks such as ostium sphenoidale, sphenoid sinus septations, optic canals, floor of sella turcica, carotid arteries, basilar artery etc. will be provided such as to enhance the 3-D information and safety during endoscopic procedures. *Conclusion:* Optical distorsion and lack of stereoscopic vision of current encoscopic systems can be reliably supplemented by a CT-based image guidance system using electromagnetic field tracking technology.

H-05

Endoscopic Management of Intracranial Arachnoid Cysts. A review of 15 cases.

N Russell (Riyadh), A Al Ferayan (Riyadh), M Al Wohaibi (Riyadh), A Al Arifi (Riyadh)*

Background: Arachnoid cysts are benign intra-arachnoid fluid collections. They occur through out the craniospinal axis, (Sylvian region predominates) and account for approximately 1% of intra cranial mass lesions. They may be asymptomatic,produce subtle symptoms or cause elevated intrcranial pressure, focal deficits and seizures. Controversies regarding their management include the indications for surgery and the selection of the appropriate procedure. *Methods:* A retrospective study of the details of 15 cases of intra cranial arachnoid cysts treated by endoscopic fenestration. *Results:* Improvement was experienced in 12/15 patients. *Conclusions:* Endoscopic treatment is a promising alternative to shunting or microsurgery for intracranial arachnoid cysts. It may be considered the intervention of first choice for these lesions

H-06

Prediction of hearing preservation in vestibular schwannoma removal by the retrosigmoid approach

*D Rowed** (Toronto), J Nedzelski (Toronto), J Chen (Toronto), D Houlden (Toronto)*

Background: Ipsilateral hearing preservation is desirable in the surgical removal of vestibular schwannomas. We analyzed our consecutive series of hearing preservation attempts for the quality of hearing preserved and for predictors of successful outcome. *Methods:* 155 consecutive retrosigmoid craniotomies were reviewed retrospectively. Preoperative hearing, mean extracanalicular tumor diameter, patient age and intraoperative cochlear nerve function ,as monitored by transtympanically recorded cochlear action potentials (CAP) and by BAEP, were some of the potential predictors examined. *Results:* Preservation of Gardner and Robertson grades 1 and 2 hearing (serviceable) occurred in 51 of 155 (32.9 percent). Tumor size correlated with outcome (p equal to 0.01). 13 of 25 (52.0 percent) of intracanalicular tumors had grade 1 or 2 hearing postoperatively compared with 38 of 130 (29.2 percent) of larger tumors (p less than 0.05 percent). CAP threshold increase equal to or greater than 20dB correlated highly with nonserviceable (equal to or greater than grade 3) hearing (p less than 0.0001). *Conclusions:* Preoperative tumor size, particularly in the case of intracanalicular tumors, and intraoperative CAP threshold increase are significant predictors of serviceable postoperative hearing.

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H-07

How patients with brain tumor present to the clinician

C DeSilva (London), R Hammond (London), J Megyesi (London)*

Background: In recent years data registries such as CBTRUS (Central Brain Tumor Registry of the United States) have been better defining the incidence and prevalence of brain tumors in the populace. This study revisits the differences in clinical presentation of those people affected by a brain tumor. *Methods:* Two hundred cases of patients with an intracranial mass lesion that had a pathological diagnosis determined at the London Health Sciences Centre between 1999 and 2004 were identified. Final pathological diagnoses for these lesions were then classified into seven categories: high grade glioma (HGG), low grade glioma (LGG), metastasis, meningioma, lymphoproliferative disorder (LPD), abscess and reactive tissue. Information including age, sex, duration of symptoms from onset to presentation and nature of symptoms were collected for each case from the initial clinical assessments of these patients. Statistical analysis was performed on the data. *Results:* The 200 cases identified included 103 males and 97 females with a mean age of 58.2 years. Patients with HGG had an average age of 63.1 years and were more likely to be male (62%). The most common symptoms were focal neurological deficit (70%), cognitive dysfunction (34%) and headache (22%). Mean duration of symptoms was 1.9 months. Patients with a LGG had an average age of 42.7 years and were more likely to be female (56%). The most common symptoms were seizures (67%) and focal neurological deficit (30%). Mean duration of symptoms was 6.2 months. Patients with metastases had an average age of 59.4 years and were more likely to be female (55%). The most common symptoms were focal neurological deficit (68%) and headache (36%). Mean duration of symptoms was 1.4 months. Patients with a meningioma had an average age of 56.6 years and were more likely to be female (62%). The most common symptoms were seizures (54%), focal neurological deficit (35%), headache (23%) and cognitive dysfunction (23%). Mean duration of symptoms was 8.3 months. Patients with a LPD had a mean age of 65.2 years and were more likely to be male (55%). The most common symptoms were focal neurological deficit (45%) and headache (27%). Mean duration of symptoms was 2.6 months. There were insufficient cases of reactive tissue (7) or abscess (3) to perform a meaningful analysis. Statistical analysis revealed the following: (1) patients with LGG are younger at presentation than patients with HGG, metastases, meningioma or LPD; (2) patients with LGG and meningioma have a longer duration of symptoms at diagnosis than HGG or metastases; and (3) patients with malignant lesions such as HGG and metastases tend to present with focal neurological deficits while patients with more indolent lesions such as LGG and meningioma tend to present with seizures. *Conclusions:* When compared to older studies of a similar nature the results of this contemporary study correlate with many, but not all, of the characteristics associated with the clinical presentation of patients with brain tumor identified in the older studies.

H-08

Does posterior fossa decompression improve oculomotor and vestibulo-ocular manifestations in Chiari 1 malformation?

W Liebenberg (Haywards Heath), A Demetriades (Oxford), C Hardwidge (Haywards Heath)*

Introduction: Only one report on the effectiveness of posterior fossa decompression on relieving oculomotor and vestibulo-ocular manifestations due to Chiari 1 malformation. We wanted to add to the literature and counsel our patients. *Methods:* Retrospective case note review. Forty consecutive patients were included over a 6 year period. *Results:* Mean age 31.5 years (13 - 62), 10 female, 3 male. 32.5% (13/40) oculomotor and vestibulo-ocular manifestations. Symptoms 8 patients (oscillopsia 3, diplopia 2, blurred vision 2, floaters 1) clinical signs 11 (nystagmus 6, nervus abducens palsy 2, increased blind spot 2, papilloedema 1, jerky pursuit 1), symptoms and no signs 2 (bilateral oscillopsia, blurred vision) Complete resolution 9/13 (69.2%) partial in 1 - 10/13 (76.9%). Mean time span to complete resolution 14.2 months (3 - 71 months) Krupina (2003) - occulomotor deficits in 17.1% cochlear vestibulocerebellar deficits in 84.4% Milhorat (1999) - ocular manifestations 78% otoneurological manifestations 74%. Spooner (1981) improvement following posterior fossa decompression 3/5 complete resolution 1/5 partial resolution. *Conclusions:* Posterior fossa decompression appears to be highly effective in causing complete resolution of disabling oculomotor and vestibulo - ocular manifestations in most cases of CM 1.

NEURO-ONCOLOGY

I-01

Regulation of glial cell polarity and invasion by Drr1

K Petrecca (Montreal), R Waldkircher (Montreal), A Angers-Loustau (Montreal), J Wang (Montreal), R Del Maestro (Montreal)*

The K.G. McKenzie Prize in Basic Neuroscience Research winner - Canadian Neuroscience Society (See page 5)

I-02

Enhanced chemotherapy delivery by intra-arterial infusion and blood-brain barrier disruption in cerebral metastasis

Cathy Gendron (Sherbrooke), Marie Boudrias (Sherbrooke), Marie-Pierre Garand (Sherbrooke), David Fortin (Sherbrooke)*

Multiple cerebral metastases are usually treated by radiotherapy as a palliative modality. There is no consensus for the role of chemotherapy delivered by intra-arterial infusion with blood-brain barrier disruption (BBBD) in this disease. In this report, we detail our experience so far with the procedure in patients with cerebral metastasis. This prospective phase II study enrolled 40 patients from November 1999 to October 2004, distributed in 5 groups based on histology of the cerebral metastasis. All patients were treated with intra-arterial chemotherapy with or without BBBD. Mean and median survival was as follows for each group: 24,4 and 16,3 months for systemic lymphoma with brain metastasis, 7,6 and 6,1

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months for breast carcinoma patients, 12,9 months and 13,4 months for lung metastasis, and 24,2 and 23,9 months for patients with ovarian metastasis. In lung metastasis specifically, a mean and median survival of 10.8 and 11.2 months was observed for patients with small cell carcinoma and 14.2 and 13.4 months of mean and median survival for patients with adenocarcinoma. We conclude that this modality of treatment is of interest in some histology, most notably ovarian carcinoma and lung small cell carcinoma and adenocarcinoma.

I-03

New pre-operative fMRI and intra-operative tools for the assessment of higher cognitive functions in patients with gliomas

C Amiez (Montreal), AS Champod (Montreal), P Kostopoulos (Montreal), M Petrides (Montreal), L Collins (Montreal), J Doyon (Montreal), R Del Maestro (Montreal)*

The objective of this study is to develop new pre-operative functional Magnetic Resonance Imaging (fMRI) and intra-operative behavioural tools to assess higher cognitive functions in patients with gliomas. Pre-operatively, we used two fMRI protocols. The first one was used to assess conditional visuomotor association function in four patients with gliomas invading the premotor cortex. The second one was used to assess mental rotation function in three patients with gliomas invading the parietal cortex. Pre-operative fMRI results demonstrated that specific regions close to the patients' tumour were involved in the tasks (i.e premotor cortex in patients tested on the visuomotor association protocol and parietal cortex in patients tested on the mental rotation protocol). Intra-operatively, the patients were regularly tested on the task that was used during the pre-operative fMRI. This behavioural assessment allowed the neurosurgeon to verify whether the higher cognitive processes were preserved throughout the surgery and to adapt the surgical approach in order to minimize the potential deficits post-operatively. Ultimately, this procedure will become a useful clinical tool since it allows an optimal tumour resection with the minimal neurological deficits. The use of this new procedure could become crucial for the patients' post-operative quality of life and autonomy.

I-04

The Syngeneic Fischer/F98 Rat Glioma Model: Standardization of the Implantation Technique and Detailed Clinical. Pathological, Radiological and Metabolic Characterization

David Fortin (Sherbrooke), David Mathieu (Sherbrooke), Roger Lecomte (Sherbrooke), Jacques Rousseau (Sherbrooke), Ana Maria Tsanaclis (Sherbrooke), Annie Larouche (Sherbrooke)*

Adequate animal glioma models are mandatory for the pursuit of preclinical research in neuro-oncology. Many implantation models have been described, but none perfectly emulate human malignant gliomas. This work reports our experience in standardizing, optimizing and characterizing the Fischer/F98 glioma model. F98 cells were implanted in 70 Fischer rats, varying the quantity of cells and volume of implantation solution, and using a micro-infusion pump to minimize implantation trauma. Twelve animals were used for MR imaging at 5, 10, 15 and 20 days. Two animals underwent 18F-FDG and 11C-acetate PET studies for metabolic characterization of the tumors. Implantation with 1x104 cells produced a median survival of 26 days and a tumor take of 100%. Large infiltrative neoplasms with a necrotic core were seen on H&E. Numerous mitosis, peritumoral infiltrative behavior, and neovascular proliferation were also obvious. GFAP and vimentin staining was positive inside the tumor cells. Albumin staining was observed in the extracellular space around the tumors. CD3 staining was negligible. MR images correlated the pathologic findings. 18F-FDG uptake was strong in the tumors on PET scan. The standardized model described in this study behaves in a predictable and reproducible fashion, and could be considered for future pre-clinical studies.

I-05

MR Imaging of F98/ Fischer glioma rats with a clinical magnet and antenna:radio pathological correlation

Jocelyn Blanchard (Sherbrooke), David Mathieu (Sherbrooke), Yves Patenaude (Sherbrooke), David Fortin (Sherbrooke)*

This study reports our findings in assessing and validating tumor growth with MR imaging using a commercial magnet and antenna in F98 implanted Fischer rats. F98 cells were implanted in 12 Fisher rats. Four groups were created to assess tumor volume at different times. Each animal underwent one MR study on a 1.5T human Siemens. Using a small loop antenna, a coronal spin echo T1 weighted MRI scan with Gadolinium was performed using pre-defined parameters. A comparison of T1 gadolinium coronal MR scans and pathology specimens in corresponding animals was accomplished. The MR enhancement areas obtained were 2.18mm^2 at 5, 8.25mm^2 at 10, 21.6mm^2 at 15 and 23.17mm^2 at 20 days. Tumor margin measurements at pathology produced areas of 0.29mm^2 at 5, 4.43 mm^2 at 10, 8.3mm^2 at 15 and 12.9mm^2 at 20 days. The T1-enhancing images constantly overestimated tumor size. This phenomenon is explained by different mechanisms: enhancement of the brain around tumor area, extra-axial tumor growth and a pathology shrinking factor of 17% related to the fixation process. Nonetheless, the radiological tumor growth reported in this study paralleled the histological samples. This technology is thus suitable to follow in vivo tumor growth in implanted rats.

I-06

Molecular Magnetic Resonance Imaging (mMRI) of Gliomas

S Assadian (Montreal), BJ Bedell (Montreal), S Mzengeza (Montreal), A.C Evans (Montreal), RF Del Maestro (Montreal)*

Background: Numerous factors, such as vascular endothelial growth factor (VEGF) and matrix metalloproteinases (MMPs), are associated with tumor angiogenesis and invasion and have become a central focus of novel targeted therapies. We have developed a novel class of molecular MRI (mMRI) probes to evaluate the expression of these targets in vivo. Quantitative analyses following administration of the probes, which act by modulating the tumor microvascular permeability, provide an estimate of the tissue content of the molecular target. *Methods:* C6 spheroids were implanted into

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cerebral hemispheres of Sprague Dawley rats. Two weeks post-implantation, the animals were imaged using a 1.5 T MRI scanner. T1-weighted images were acquired following intravenous administration of the probe and quantitative maps of protein expression were generated. Protein expression was also determined on tissue sections. *Results:* Quantitative MR maps successfully demonstrated the expression of the molecular targets and correlated well with the histology data. These studies also demonstrated the ability of these probes to detect temporal changes in the mediators of angiogenesis and invasion. *Conclusions:* These novel probes allow for in vivo MR imaging of the expression of various molecular targets localized to gliomas and should find numerous applications, including the evaluation of targeted therapeutic agents.

I-07

Childhood craniopharyngioma: a conservative approach.

J Hukin (Vancouver), J Visser (Vancouver), M Sargent (Vancouver), K Goddard (Vancouver), C Fryer (Vancouver), P Steinbok (Vancouver)*

Background: Management of craniopharyngioma at our center has involved a relatively conservative surgical approach, designed to control tumor growth while attempting to limit morbidity of the treatment and tumor. *Methods:* We retrospectively reviewed the records and neuroimaging of all children diagnosed with craniopharyngioma between 1982 and 2003. *Results:* The initial intervention was acute decompression of hydrocephalus and/or cyst drainage only, in 22/29. Definitive therapy was resection (9), resection and radiation (9), radiation alone (3) and intracystic bleomycin (8). 3/9 patients who had surgical resection as the only definitive treatment, have required no further intervention. After bleomycin, all 8 responded, with complete response in 3. 3/8 have not required additional therapy, and radiation was delayed by a median of three yrs (range 1-9). Deficits at a median follow-up of eight years include: panhypopituitarism 93%; visual 68%; cognitive 32%. 10 yr progression free survival is 35% (95% CI: 14%, 56%). 10 yr overall survival is 80% (95% CI: 61%, 98%). *Conclusions:* Most children with craniopharyngioma are long-term survivors, but have multiple deficits. A conservative surgical and radiotherapeutic approach may minimize these. Use of intracystic bleomycin delays more aggressive therapies in select patients.

I-08

Navigating the posterior fossa:image-guidance in the treatment of posterior fossa tumors

*R Leblanc** (Montreal), AM Zeitouni (Montreal), L Soualmi (Montreal)*

Introduction: We describe our experience with image-guidance in the treatment of posterior fossa tumors and present selected cases illustrating the usefulness of neuronavigation in the treatment of these lesions. *Methods:* We used neuronavigation based on the pre-operative localization of standardized anatomical structures and with novel software for enhanced vascular reconstruction in the surgery of over 50 intra- and extra-parenchymal posterior fossa tumors. *Results:* Neuronavigation helps in determining the best approach to the tumor and in positioning the patient to achieve maximal exposure of the lesion. It allows the delineation of the anatomical margins of the tumour in three dimensions; and identifies the transverse and sigmoid sinuses in the initial approach to the tumor. It is also instrumental, as the resection proceeds, in identifying the relationship of the tumor to important structures and landmarks such as the brain stem, the tentorial notch, and the acoustic meatus. These features will be highlighted in the presentation of interesting cases of small, large, and cystic acoustic nerve tumors, schwannomas of the trigeminal nerve, tentorial meningiomas, and cerebello-pontine angle hemangioblastomas. *Conclusions:* Image-guidance is helpful in the treatment of posterior fossa tumors, especially schwannomas of the Vth and VIIth nerves and meningiomas.

Multiple Sclerosis

J-01

Increased frequency of the restless legs syndrome in multiple sclerosis.

C Auger (Montreal), P Duquette (Montreal), P-O Despault-Duquette (Montreal)*

Background: The restless legs syndrome (RLS) can be primary, or secondary. For primary RLS, 3 genetic loci have been identified. We have previously reported preliminary data indicating an increased frequency of RLS in multiple sclerosis (MS). We have completed a larger study on this association. *Methods:* Using a questionnaire based on the four diagnostic criteria established by the International RLS Study Group, we have compared the frequency of RLS between 200 MS patients, 100 rheumatoid arthritis (RA) patients, and 100 healthy subjects. Only subjects fulfilling the four criteria were considered. *Results:* The frequency of RLS was of 37.5% in the MS group, 31% in the RA group, and 16% in the healthy group. The difference between the MS and the healthy group was significant (p value : 0,0001). 30% of patients with both MS and RLS have a positive family history of RLS. *Conclusions:* In the French Canadian population, MS patients have an increased frequency of RLS. We are conducting studies to evaluate whether this association is based on common genetic factors, or whether MS will be added to the list of diseases associated with RLS. We will also evaluate the response to recommended symptomatic agents.

J-02

Incidence of multiple sclerosis (MS) among First Nations people compared to the general population of Alberta

LW Svenson (Edmonton), S Warren (Edmonton), KG Warren (Edmonton), LM Metz (Calgary), DP Schopflocher (Edmonton)*

Background: MS is reported to be uncommon among North American aboriginals, although few systematic studies have been conducted. This study's purpose was to describe the incidence of MS among First Nations people of Alberta compared to the general population. *Methods:* All fee-for-service and hospital records for 2002 which mentioned a diagnosis of MS were extracted from Alberta Health Care Insurance Plan (AHCIP) data. An individual was considered a case if they had had 2 or more physician visits for MS or 1 or more hospitalizations. First Nations can be identified

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since Health Canada pays insurance premiums on their behalf. A case was considered incident if there was no record of services for MS in the previous 5 years. Incidence rates (95% confidence limits) were calculated per 100,000 population, age-standardized to the 1996 Canadian population. *Results:* The 2002 incidence rate for First Nations was 7.6/100,000 (2.6-12.7) and for the general population 20.6/100,000 (18.9-22.2). Rates were more than double for females among both First Nations and the general population. *Conclusion:* While the incidence rate for First Nations people was not as high as for the general population, MS incidence among First Nations in Alberta cannot be described as rare by worldwide standards.

J-03

Hydroxychloroquine: From bench to bedside

R Zabad (Calgary) , R Lewkonia (Calgary) , L Metz (Calgary) , V Yong (Calgary)*

Background: Hydroxychloroquine (HQ), an antimalarial agent, is endowed with many immunomodulatory properties. Because of the latter, we examined the effect of HQ in the context of models of MS. *Methods:* Cultured microglia from fetal and adult human brains were pretreated with HQ and cells were then stimulated with lipopolysaccharide (LPS) or activated T cells. TNF-alpha and IL-10 production was then measured. For in vivo experiments, C57BL/6 mice were pretreated with HQ (100 mg/kg) intraperitoneally, and EAE was then induced with a myelin protein (MOG); animals were sacrificed 14 days after. *Results:* In culture, HQ significantly decreased TNF-alpha and IL-10 production by activated microglia. In animals, EAE in vehicle pretreated mice developed by days 10-12 after MOG immunization. However, in animals pretreated with HQ, animals had not yet developed disease at 14 days post-MOG. Histological analysis showed less inflammation and demyelination and no signs of microglia activation in the HQ group. *Conclusion:* HQ decreases many parameters involved in the pathogenesis of EAE and MS. It is possible that HQ may play a role in MS modulation. Our plan is to test HQ in clinically isolated syndrome to determine whether the conversion to MS can be delayed.

J-04

Measurement of Axon Loss in Optic Neuritis with Optical Coherence Tomography

F Costello (Ottawa), S Coupland (Ottawa), G Lorello (Ottawa), J Koroluk (Ottawa), R Kardon (Ottawa), D Zackon (Ottawa)*

Background: Optic neuritis (ON) is a demyelinating injury of the optic nerve, which frequently manifests with painful vision loss, a relative afferent pupil defect, dyschromatopsia, visual field loss, and a normal fundus appearance at the time of presentation. The retinal nerve fiber layer (RNFL) lacks myelin, and therefore thinning of this portion of the anterior visual axis correlates to axon loss. Retrobulbar optic nerve injuries manifest with fundus findings over time, which include RNFL defects and optic disc pallor. Optical coherence tomography (OCT) may be used to measure RNFL thinning and hence axon loss after an acute ON event. With use of this optical imaging technique, it is possible to quantify axon loss in optic neuritis, as a system model of demyelination within the central nervous system. *Methods:* In this case series, patients with suspected unilateral underwent a standard neuro-ophthalmic examination at presentation and in follow up. This included assessment of best-corrected visual acuity (VA), relative afferent pupil defect (RAPD), colour vision (Ishihara plates), Humphrey perimetry and dilated ophthalmoscopy. All patients underwent OCT testing (Stratus Version 3) for measurement of RNFL (3.4) thickness at presentation and during the course of their recovery. Selected patients underwent mfERG (VERIS Version 4.3), cranial magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis, and visual evoked potential (VEP) testing. *Results:* Sixty-three patients (48 females, 15 males) were diagnosed with ON. The mean age of the ON patients was 36 years (range 13-61 years). The right eye was affected in 51% of patients with ON. The ON patients typically presented with pain (87%), decreased VA (69%), an ipsilateral RAPD (100%), dyschromatopsia (90%), a RNFL pattern of visual field loss (98%) and a normal fundus examination (65%). At follow up (mean 12.5 months, range 1- 82 months), the majority of ON patients developed optic disc pallor (83%) and demonstrated visual improvement (79%) over time. Seventy eight percent of patients achieved a Snellen visual acuity of 20/40 or better in the affected eye. In this group, 89% of patients (27) tested had an abnormal VEP, and 86% had thinning of the RNFL in the affected eye after a minimum of 3 months of follow up. Thinning of the RNFL in the affected eye tended to occur between 3 to 6 months after the acute ON event, and no patients tested less than 3 months after the ON event manifested RNFL thinning in the affected eye. During the course of follow up, 4 patients demonstrated RNFL losses in the contralateral eye, which was consistent with sub-clinical ON. Among the 11 patients with relatively poor visual recovery, there was more extensive thinning of the RNFL (< 70 microns) in the affected eye as compared to patients with better visual outcomes. Among the ON patients, 69% had abnormal cranial magnetic resonance imaging results. *Conclusions:* Optical Coherence Tomography is a useful ancillary test, which can help quantify the extent and rate of axon loss among patients with optic neuritis. In this study, the vast majority of patients with optic neuritis demonstrated axon loss after the acute onset of vision loss. Those patients with more extensive axon loss demonstrated less visual recovery over time, and this axon loss was the presumed substrate of permanent visual dysfunction among patients with poorly recovered optic neuritis. The OCT is a reliable and non-invasive means of measuring axon loss in the context of optic neuritis, and provides a structural correlate to functional measures of visual performance in this "system model" of central nervous system demyelination.

J-05

A demographic study and relation between MS and serum vitamin B12 level

Parviz Bahrami (Khorramabad), Tahereh Javadi (Khorramabad)*

MS is an inflammatory relapsing remitting or progressive disorder of CNS white mater and is a major cause of disability in young adults. *Methods:* This study is a descriptive prospective research and the main aim was determination of relation between serum B12 level and MS. We evaluate serum B12 level and demographic characteristic of patients by a questioner form.The data were collected and evaluated by SPSS program and T-test. *Finding:*

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total patients were 66(44 female and 22 male) and only 38 patients participated in this study. Mean age was 32.8 years. The most common range of age was between 21-40 years old. 26 patients (68.4%) were female and 12(31,6%) male. F/M ratio was 2/1. The peak onset of disease was 3rd decade (65.8) and 2.6% in 34 years old. The first symptom was pyramidal sign in 24 patient (63.2%)and visual problem in 13 (34.2%) patients, and speech disorder in 2.6% of patients. The most common findings in order include: pyramidal, visual, sensory symptom, unsteadiness and incontinency. 68.4% had pain (back, limbs pain and headache). In 10 person (26.3%) was family relative in their parents. Blood group: 34.2% had BG O, 29% A, 18.4% B and 18.4% AB.92% were Rh + and 8% Rh negative. Serum B12 level was normal in 24 patient (63.2%) and slightly lower than normal in 14 patients (36.8). *Conclusion:* The most patient had normal serum B12 level and we did not find clear relation between B12 and MS.

J-06

Mercury and MMP-9: A Possible Link to MS?

TR Todoruk (Calgary), L Metz (Calgary), VW Yong (Calgary)*

Background: Matrix metalloproteinases (MMP) have been implicated in the pathogenesis of neurological disease. In multiple sclerosis (MS), MMP-9 may play an important role in disease development and progression. MS is caused by a combination of genetic and environmental factors. *Methods:* MMP-9 activity was measured using a fluorogenic activity assay. T cells were isolated using FICOLL® extraction protocols. Disease was induced in mice using suboptimal myelin oligodendrocyte glycoprotein (MOG) and low dose mercury (Hg) pretreatment. Mice were scored using a 15 point system. *Results:* We have elucidated a potential environmental factor, Hg, in conjunction with MMP-9 as playing a role in the onset and/or progression of MS. Active MMP-9 shows increased activity in the presence of Hg; this plays a role in activation of T cells. In vivo studies on mice exposed to low dose Hg and suboptimal dose MOG show greater EAE severity, but only when the MMP-9 gene is present. Pathology supports a worse neurological outcome in Hg exposed mice. Associative epidemiological data, correlating mercury pollution with MS prevalence, supports a role for Hg in MS. *Conclusions:* Hg in combination with MMP-9 plays a role in inflammatory processes and can affect EAE onset and severity and may affect MS.

STROKE

K-01

Hypertension and stroke: 2005 CHEP (Canadian Hypertension Educational Program) recommendations.

JM Boulanger, on behalf of the CHEP (Canadian hypertension educational program) (Calgary)*

Background: Hypertension is the leading cause of stroke. The CHEP (Canadian Hypertension Educational Program) represents Canada's experts in the field of hypertension. It publishes annual evidence-based recommendations on the diagnosis and treatment of hypertension. *Methods:* We present the 2005 CHEP guidelines regarding the management of hypertension in patients with stroke. *Results:* The diagnosis of hypertension should be expedited and can be made as early as the second visit in patients with stroke. Unless contraindicated, a combination of angiotensin-converting-enzyme (ACE) inhibitors and diuretics is the preferred therapy in these patients. A blood pressure (BP) below 140/90mmHg should be obtained. For diabetic patients with stroke, a tighter control (130mmHg/80mmHg) is suggested; even more so in those with proteinuria and diabetes (125mmHg/75mmHg). ACE inhibitors are not recommended for black patients and other classes of agents should therefore be used. Lifestyle interventions are also effective in the management of hypertension. Waist circumference should be below 102cm for men and 88cm for women. There is uncertainty about the management of high blood pressure in the context of acute stroke. *Conclusions:* A combination of ACE-inhibitors and diuretics is recommended in hypertensive stroke patients. Blood pressure should be maintained at least below 140/90 mmHg.

K-02

Indolent course and late recurrence of isolated angiitis of the CNS

Stanley Elysee (Montreal), Daniela Toffoli (Montreal), Sylvain Lanthier (Montreal)*

Background: 29% of adults receiving immunosuppressive therapy for isolated angiitis of the CNS (IACNS) experience recurrences within 4 years. No longitudinal study of childhood IACNS has been published. *Methods:* Case report. *Results:* A 10-year-old child presented in February 1992 with left-sided seizures and hemiparesis. MRI revealed infarcts in the right middle and posterior cerebral artery territories. Blood and CSF analyses were unremarkable. Cerebral angiography showed a single right middle cerebral artery stenosis. CNS biopsy demonstrated non-granulomatous vasculitis. She received anticonvulsants for 6 months, prednisone 2 mg/kg/day for 22 months, and oral cyclophosphamide 2 mg/kg/day for 20 months. In July 2001, she presented with left-sided seizures. She reported progressive left-sided tremor and stiffness since 1997. Examination showed spastic left-sided hemiparesis, rubral tremor, hemisensory deficit and hemianopia. MRI disclosed new right pallidal, frontal and occipital infarcts. Blood and CSF analyses and cerebral angiogram were unremarkable. EEG revealed occipital spikes-and-waves. She received prednisone 1 mg/kg/day for 6 months, pulses of IV cyclophosphamide 1 gm/kg/month for 8 months, and anticonvulsants. Repeat MRI showed no additional cerebral lesion and she remained asymptomatic as of December 2004. *Conclusions:* IACNS can sustain an indolent course with prolonged disease-free intervals and recurrences after favourable initial response to immunosuppressive therapy.

K-03

Minocycline-based drug cocktail: efficient neuroprotection in experimental transient and permanent ischemia

J Kriz (Quebec), YC Weng (Quebec)*

At the present there is no efficient pharmacological treatment for stroke. Considering that several pathways leading to a cell death are activated in cerebral ischemia, effective neuroprotection may require

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the combination of drugs that target distinct pathways during the evolution of ischemic injury. We tested a drug cocktail consisting of minocycline- an antibiotic with anti-inflammatory properties, riluzole - a glutamate antagonists, and nimodipine, a voltage-gated calcium channel in a mouse models of transient and permanent ischemia. When first administered 2 hours after stroke, the three-drug treatment reduced the size of infarction by 60% following transient and 35% after permanent middle cerebral artery occlusion -significantly better than minocycline, riluzole or nimodipine alone. 7 days after transient ischemia the size of infarction was reduced by 55% in treated animals. These effects were associated with markedly improved clinical recovery of mice and by the reduced immunoreactivity for markers of microgliosis and apoptosis following transient ischemia. Interestingly, the results of our study also revealed marked differences in tissue response to ischemic injury and to the anti-glutaminergic treatment in permanent vs. transient ischemia. However, the three-drug cocktail exerted significant neuroprotection in both experimental models and thus may represent an effective therapeutic strategy for stroke.

K-04

Informed consent for thrombolysis in acute ischemic stroke - current dilemma

V Palumbo (Calgary), C Sivakumar (Calgary), J Roy (Calgary), S Subramaniam (Calgary), JM Boulanger (Calgary), M Hill (Calgary), A Buchan (Calgary)*

Background: Majority of acute stroke patients have diminished capacity for consent. Surrogate consent has legal and logistic issues. Protocol violators have increased risk of hemorrhage. We sought to find out the current scenario of informed consent. *Methods:* We prospectively collected data on 108 acute ischemic stroke patients. Capacity for consent was presumed if patients were alert, orientated and had no aphasia or neglect. Instances of surrogate consent were tested for appropriateness to patient's capacity for consent. *Results:* Consent was obtained and documented in 83/108 (77%) patients. There was no documentation in the chart for 25/108 (23%) subjects. Median baseline NIHSS score was 14 (range 0-42), 42% were "protocol violators". Capacity for consent was present in 21/108 (20%) of whom 8/21(38%) had surrogate consent. Diminished capacity was found in 87/108 (80%) of whom 8% consented themselves. 12/87 (14%) of the patients unable to consent had two-physician consent documented. Consent by patient was appropriate in 12/21 (57%) and inappropriate (due to diminished capacity) in 7/87 (8%). Surrogate consent was appropriate in 43/87 (49%) and inappropriate in 8/21 (38%). *Conclusion:* The documentation of capacity for consent is sub-optimal. In a substantial minority of patients, the consent process was inappropriate.

K-05

Visualization of penumbra in human cerebral ischemia by CT perfusion

MJ Hogan (Ottawa), A Srinivasan (Ottawa), M Sharma (Ottawa), C Lum (Ottawa), M Goyal (Ottawa)*

Background: Measurement of regional cerebral blood flow (CBF) and blood volume (CBV) during acute stroke may identify both the infarct core and the potentially salvageable ischemic penumbra and may be obtained with CT perfusion imaging during the initial CT evaluation of acute stroke patients. *Methods:* Fifteen subjects referred for CT perfusion studies within 6 hours of stroke onset and who also had subsequent CT imaging defining the extent of final cerebral infarction were reviewed. CBV and CBF maps were displayed using standardized color scales and regions were categorized as having a severe or partial reduction of CBV and CBF based on color appearance. CBF-CBV mismatch was defined as the difference in spatial extent between regions with any CBF reduction and regions with severe CBV reduction (sCBV) and the overlap with the extent of final infarction examined. *Results:* Acute infarct was identified in 14 subjects affecting 11% (1% to 63%) of the cerebral hemisphere area. sCBV was observed in 8 subjects and 7 had infarction with 92±11% of the sCBV region lying within the infarct. CBF-CBV mismatch regions were identified with only 21±20% of the reduced CBF region overlying the region of sCBV. The extent of these mismatch regions progressing to infarction was 50±23%. *Conclusion:* A significant region of CBF-CBV mismatch was observed in which the progression to infarct was variable. This region can be rapidly identified with CT methods and may represent the ischemic penumbra.

K-06

Albumin therapy for ischemic stroke: The ALIAS phase I dose-escalation and safety trial

M Hill (Calgary), M Ginsberg (Miami), Y Palesch (Charlston), K Ryckborst (Calgary), D Tamariz (Miami)*

Background: Human albumin (ALB) therapy is highly neuroprotective in preclinical models of cerebral ischemia. *Design:* ALB (25% solution) was administered within 16h of stroke onset to subjects with acute ischemic stroke and NIHSSSe6 in a dose-escalation design. Two cohorts were assessed, with and without tPA treatment. Seventy subjects have been enrolled into 5 ALB dose-tiers from 0.34 g/kg to 1.71 g/kg. Outcome was assessed (mRS, Barthel, NIHSSS) at 1 and 3 months. *Results:* Mean age (SD) was 66 (15) years; 38 were male. The 2-h ALB infusion was begun at 8.2(3.7)h after stroke onset. Six subjects died; all had severe strokes (NIHSSS 23-38). Pulmonary edema occurred in 3 subjects of tier IV (but in none of tier V, when prophylactic furosemide was encouraged). One serious adverse event (SAE) (congestive failure with prolonged hospitalization) in tier III was possibly ALB-related. No tier IV or V subject had ALB-related SAE's. A dose-by-tPA administration interaction was suggested such that patients in the higher dose tiers who received tPA were much more likely to have a good outcome. *Conclusions:* ALB therapy is well tolerated, and higher-dose ALB may improve neurological outcome. A Phase III trial - the ALIAS trial - is planned.

K-07

Catheter navigation, thrombolysis and stenting of acute symptomatic cervical internal carotid artery occlusion

C Lum (Ottawa), P Stys (Ottawa), M Sharma (Ottawa), A Srinivasan (Ottawa), M Hogan (Ottawa), M Goyal (Ottawa)*

Background: The treatment of acute anterior circulation stroke

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distal to an occluded cervical internal carotid artery at the common carotid artery bifurcation (cICA) presents a challenge. There is evidence suggesting treatment only with iv-tPA results in poor outcomes. Case series have described some success with endovascular treatment. However, published experience is lacking regarding residual stenoses and clot at the cICA post acute thrombolysis. Since 2001, our protocol for treatment for acute stroke presenting under 6 hours included an option for direct intra-arterial thrombolysis of large vessel (ICA,M1) clot. No patient with large vessel occlusion is denied standard iv-tpa if presenting under 3 hours. Our goal was to evaluate the outcomes of patients who presented with symptoms related to cICA occlusion who underwent endovascular treatment during this period and to describe the rationale and technique for acute cICA stenting of residual clot/stenosis post thrombolysis. *Methods:* All patients presented < 6 hours from stroke onset. CT angiography and perfusion studies were performed to confirm location of clot and to estimate the degree of penumbra. When possible, iv-tPA was given prior to endovascular treatment. The techniques for vessel recanalization were analyzed. Post-procedure CT scans were reviewed for hemorrhage. Outcomes were assessed using the modified Rankin scale (mRS). Good outcomes were assigned an mRS <=2. *Results:* Over a 2 year 3 month period, a total of 24 patients underwent endovascular treatment for acute stroke under this protocol. 6 patients had cICA clot. 5 of 6 had pre-procedure non-invasive imaging studies confirming the occluded ICA and perfusion studies suggesting a large penumbra and significant neurological symptoms related to the affected hemisphere. 5 of 6 had clot in the MCA distal to an occluded ICA, one patient occluded at the origin of the ICA post-endarterectomy. All were treated with intra-arterial tPA through a catheter advanced through the occluded ICA. Three/6 underwent acute ICA stenting for flow across residual cICA clot/stenosis. Two/6 had angioplasty of MCA clot. 4 of 5 patients in which TIMI 3 flow was achieved had good outcomes, one patient had mRS=3, one patient mRS=5. There were no deaths. One patient who did not undergo stenting had an asymptomatic intracranial bleed. *Conclusion:* Thrombolysis of intracranial clot through an occluded ICA is feasible, with a low morbidity and may be associated with good outcomes. In this series, acute cICA stenting was not associated with any adverse events.

K-08

Carotid angioplasty and stenting in high-risk patients

G Redekop (Vancouver), D Graeb (Vancouver), C Haw (Vancouver), R Heran (Vancouver)*

Background: Carotid endarterectomy is the current gold standard treatment for extracranial carotid stenosis. Percutaneous intervention with angioplasty and stenting is a minimally invasive alternative to surgery and may offer advantages to patients at higher risk for endarterectomy because of medical or anatomical considerations. *Methods:* A series of 86 consecutive high-risk patients undergoing angioplasty and stenting for atherosclerotic narrowing of the extracranial carotid artery is presented. 78 (91%) were symptomatic, 6 were asymptomatic, and 2 required stenting to facilitate access for endovascular therapy of symptomatic intracranial aneurysms. Patients were evaluated pre- and post-operatively by a neurologist and had non-invasive imaging follow-up at 6 month intervals. *Results:* There was one major procedural stroke (1.2%), two minor ischemic events that resolved within 24 hours (2.3%), and one myocardial infarction (1.2%). Total neurological and cardiac morbidity and mortality was 4.7%. Two patients had ipsilateral strokes 30 - 60 days after stenting; in both cases antiplatelet medications had been discontinued. No delayed ipsilateral strokes have occurred. Forty patients have been followed for more than 1 year, with one observed case of significant re-stenosis requiring further intervention (2.5%). *Conclusions:* Carotid angioplasty and stenting can be performed in high risk patients with acceptable rates of morbidity and mortality. Post-stenting antiplatelet therapy is essential. Long term follow up is necessary to determine whether protection from stroke is comparable to endarterectomy.

General Neurology

L-01

Sensory neuropathy in HIV/AIDS patients highly exposed to antiretroviral therapy: protease inhibitor-mediated neurotoxicity

JA Pettersen (Calgary), G Jones (Calgary), C Worthington (Calgary), HB Krentz (Calgary), OT Keppler (Heidelburg), A Hoke (Baltimore), MJ Gill (Calgary), C Power (Calgary)*

Frances McNaughton Memorial Prize winner - Canadian Neurological Society (See page 5)

L-02

Teaching communication skills to neurology residents: design and implementation of a resident-run program

L Cooke (Calgary), S Kurtz (Calgary)*

Background: The RCPSC has mandated formal communication skills training for specialty residents. This paper describes the design, implementation, and results of a resident-run communication initiative for neurology residents at the University of Calgary in response to that mandate. *Methods:* A senior neurology resident pursuing graduate studies in medical education spearheaded this project. Data was drawn from needs assessments, participant feedback, faculty surveys, and semi-structured interviews. Critical environmental factors that facilitated implementation of this structured curriculum are described. We present the design of the curriculum and perceptions of the participants (9) and faculty. *Results:* The program was very successful. All sessions were well-attended and residents participated enthusiastically. Over time, residents began to discuss communication challenges in terms of specific skills, rather than content. Residents acknowledged giving more thought to specific communication skills from day-to-day and most expressed interest in precepting future sessions. All residents expressed the desire for the program to continue and most wanted longer sessions. *Conclusion:* It is feasible to implement a quality communication curriculum in specialty programs given a supportive milieu. Preliminary results from this project have been presented at the Ottawa International Conference on Medical Education and will be submitted to the RCPSC Annual Meeting for 2005.

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L-03

Clinicopathologic findings in an autosomal dominant neurodegenerative disorder

D Grimes (Ottawa), F Han (Ottawa), D Bulman (Ottawa), L Racacho (Ottawa), J Woulfe (Ottawa)*

Background: There is growing overlap being recognized in the clinical and pathologic diagnosis of neurodegenerative diseases. We have been studying a large family where an autosomal dominant levodopa responsive parkinsonism has been the primary feature in the majority of those affected. *Methods:* 5 individuals from one family underwent pathologic study using standard procedures including immunostaining for ubiquitin, tau, and synuclein. *Results:* 4 of the 5 individuals were felt clinically to a have typical levodopa responsive parkinsonism. Three autopsies showed neuronal loss and gliosis of the substantia nigra. In one the Lewy bodies (LB) were limited to brainstem nuclei, the second had in addition diffuse cortical LB with the third not having any synuclein positive pathology. In the fourth individual there was no neuronal loss seen within the substanstia nigra nor LB found. Instead, there were tau-based neurofibrillary lesions in the substantia nigra with very rare cortical neurofibrillary tangles and scattered neuritic plaques. Pt 5 clinically was felt to have Alzheimer's disease without parkinsonism. On autopsy there were abundant cortical tau positive tangles and beta -amyloid plaques in keeping with this diagnosis. *Conclusions*: This family suggests that a common mechanism exists that causes neuronal dysfunction that can lead to a wide range of clinical and pathologic findings; the latter encompassing both synuclein- and tau-based lesions.

L-04

Laminin enhances nerve regeneration in a tissue-engineered skin transplanted on nude mice

R Caissie (Quebec), F Berthod (Quebec)*

Background: The use of autologous reconstructed skin appears to be a promising treatment for the permanent coverage of extensive burns. However, the capability of reconstructed skin transplanted on wounds to promote recovery of tactile sensitivity is a major concern. Our aim was to develop a tissue-engineered skin that stimulates nerve regeneration. *Methods:* Our team has developed a collagen based sponge which promotes nerve regeneration. This biomaterial was enriched with laminins and Nerve Growth Factor and was used as a scaffold to grow dermis and epidermis. It was then grafted on the back of athymic mice. *Results:* Immunohistochemical studies on biopsy specimens enriched with laminin and harvested 120 days after grafting showed improved nerve regeneration potential (compared to a control group). Neurosensory recovery was evaluated by testing all three types of sensory nerve fibers (A-Beta, A-Delta and C) with a Neurometer (Neurotron Inc. Baltimore, MD). An improvement in the sensory function was observed for the A-Beta and A-Delta nerve fibers on grafts enriched with laminin. *Conclusion:* The use of a tissue-engineered autologous skin graft enriched with laminin has the potential to become an efficient solution to promote a better tactile recovery for patients.

L-05

Creutzfeldt-Jakob disease mortality in Canada: analysis of epidemiologic surveillance data for 1998-2003

HX Wu (Ottawa), E Olsen (Ottawa), A Giulivi (Ottawa), J Wu (Ottawa)*

Objective: To examine trends in mortality, resulting from Creutzfeldt-Jakob disease (CJD) in Canada during 1998-2003, through a comprehensive national surveillance program and subject the group to detailed epidemiologic analysis. *Method:* Case ascertainment was based on notifications by neurologists, neuropathologists and laboratories during 1998-2003. *Results:* A total of 182 deaths from definite or probable CJD were registered during the study period. The majority of cases were sporadic CJD (89.0%), with 4.4% GSS, 3.8% inherited, 2.2% iatrogenic, 0.6% variant CJD [the patient with variant CJD had been multiple stays in the UK during the peak of bovine spongiform encephalopathy (BSE) exposure]. The mortality rates ranged from approximately 0.80 in 1998 to 1.14 deaths per million in 2000 with an increase in the 60-69 year age group from 2.1 per million in 1998 to 5.0 in 2003. The male to female ratio was 1:1.2 ($p>0.1$). Below 40 years of age, mortality rates were extremely low. Mortality rates increased substantially in the 50-59 year age group and reached a peak of around 6 per million person-years in the 70-79 year age group. *Conclusion:* The analysis of annual CJD mortality data would be an efficient tool for monitoring incidence trends. Intensive surveillance is important in assessing events resulting from BSE or other new potential risk factors.

L-06

ALS incidence in Nova Scotia over a twenty year period

J Bonaparte (Halifax), I Grant (Halifax), T Benstead (Halifax), J Murray (Halifax)*

Background: Previous studies have suggested a relatively high incidence of ALS in Nova Scotia, and a trend toward increasing incidence over time. The purpose of this study was to determine the current incidence of ALS in Nova Scotia and to compare current data to that collected in 1984 and 1995 to determine if the incidence of ALS is changing. *Methods:* All neurologists and physiatrists in Nova Scotia were prospectively surveyed at monthly intervals during the period March 1, 2002-February 28, 2003. Diagnosis was based on El Escorial criteria for definite or probable ALS. Information collected included patient age, sex, and ALS subtype. The incidence was age-adjusted to the 2001 Nova Scotia population. *Results:* We identified 21 new ALS cases for a crude incidence of 2.24/100,000. Fourteen were male (3.05/100,000) and 7 were female (1.46/100,000). The median age at diagnosis was 58 years. Median age and sex ratio were not significantly different than in 1995. The age-adjusted incidence rate for 2003 was 2.13 (95% C.I. = 0.11-4.15), similar to the age-adjusted rate in 1995 (2.3/100,000; 95% C.I. = 0.08-4.52). *Conclusions:* The age-adjusted incidence of ALS in Nova Scotia is stable. A small trend toward increasing raw incidence is explained by an aging population and probably by improving diagnosis and by the use of retrospective methods in older studies. Ongoing data collection will evaluate the reliability of these conclusions.

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L-07

Non pharmacological treatment of migraine headache

Parviz Bahrami (Khorramabad), Ferah Dellaram (Khorramabad), Zahra Khonsari (Khorramabad)*

Headache is one of the frequent complaints heard in the offices of internists and neurologists. Migraine is a recurrent, throbbing headache. *Method:* this research is a descriptive cross-sectional study, the main goal is description of frequency of effective factors in non pharmacological treatment of migraine in 300 patients. This research have been based on type of migraine, age, sex, stimulation of vomiting, usage of calm and darkened room, usage of cool compress and massage in order to alleviate migraine headache. *Results:* 1) The most common type of migraine was common migraine and then classic, opthtalmoplegic, ergot dependent complicated and status migraine in order. 2) The most common age was third and fourth decades. 3) The ratio of female to male was 3/1. 4) In order to frequency calm and darkened room in 82%, reduce of emotional stress in 80%, stimulation of vomiting in 52%, head massage in 45%,and usage of cool compress in 32% of cases alleviate the headache. *Conclusion:* a non stressful lifestyle and use of each of the above maneuver can relieve or reduce the intensity of headache and prevent drug treatment and complication of drug .

L-08

False recognition errors during Wada memory assessment are more frequent in patients with frontal lobe seizures.

G Lee (Augusta), J Politsky (Augusta), A Murro (Augusta), C Clason (Augusta), J Wilson (Augusta), J Smith (Augusta)*

Background: Although patients with frontal lobe lesions generally have normal, or near normal, recent memory functions, such patients may have elevated false positive recognition rates during memory testing. Since false recognitions have not yet been thoroughly studied in frontal lobe epilepsy patients, we reviewed results of Wada memory assessment to determine if patients with frontal lobe seizures have more false recognition errors. *Methods:* 528 epilepsy surgery patients with complete preoperative Wada memory assessment results who subsequently had focal cortical resections in either frontal (N = 116) or non-frontal (N = 412) regions served as subjects. There were no significant differences between groups with regard to age, handedness, gender, language laterality, seizure type, laterality of onset, duration of seizures, amobarbital dose, or baseline memory ability. *Results:* Patients with frontal lobe seizures produced more false recognitions during Wada memory testing after both left ($p = .02$) and right ($p = .04$) amobarbital injections than patients with non-frontal seizures. These results cannot be due to demographic, seizure history, or Wada procedural variables since groups were equivalent. *Conclusions:* False positive errors during Wada recognition memory testing may assist with seizure onset localization in some epilepsy surgery patients when considered in conjunction with other functional tests.

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POSTER PRESENTATIONS

CEREBROVASCULAR SURGERY

P-001

Normal and perturbed laminar flow in epicerebral arteries and veins: analysis by fluorescein angiography

*William Feindel** (Montreal)*

Background: Laminar flow in the brain was noted in connection with red cerebral veins after a focal seizure or draining a cystic scar (Penfield, 1937) or vascular tumors and angiomas (Feindel and Perot, 1965). But with fluorescein angiography of the brain (FAB), laminar flow is evident in all epicerebral arteries and veins (Feindel, Yamamoto and Hodge, 1967). This report analyzes laminar flow under normal and perturbed conditions. *Method:* FAB involved the intra-arterial injection of fluorescein combined with rapid timed serial photography or video filming of the exposed brain (Hodge, Feindel, Yamamoto, 1978). *Results:* In normal vessels, laminar flow is axial and variable according to the pattern of branching. Turbulent flow and cerebral steal occur even in small angiomas. In epicerebral veins laminar flow derived from small tributaries persists to the point of entry into the sagittal sinus. Occlusion of draining veins produces reversed collateral flow and subpial hemorrhages. Freezing lesions of the cortex changes venous laminar flow patterns because of microvascular damage. In experimental ischemic stroke venous return decreased with loss of laminar flow. *Conclusions:* Laminar flow, demonstrated by FAB as a characteristic feature of epicerebral arteries and beins, is perturbed in angiomas, venous occlusion, freezing lesions of the cortex and experimental ischemic stroke.

P-002

Balancing the risk of thromboembolism with hemorrhage in patients with central nervous system hemorrhage and a strong indication for anticoagulation.

G Hawryluk (Toronto), M Fehlings (Toronto), C O'Kelly (Toronto)*

The management of anticoagulant (AC) therapies in patients with central nervous system (CNS) hemorrhage and concomitant indication for AC is a frequent and challenging dilemma. To determine the safest means of management, we performed an evidence based literature review. We selected papers in the English language subsequent to 1978 by performing a pubmed search with appropriate MeSH. This identified 18 papers reporting 288 patients with 296 bleeds associated with AC use. Following the initial hemorrhage, 4.7% had suspected or definite thromboembolic (TE) complications; 90% of these patients were on some form of anticoagulation. In two thirds, the event occurred within 10 days. No clear risk factors for TE were discernable from the data. Cessation of AC was associated with a low risk of TE complication. Hemorrhagic complications were seen in 6.6% of patients. All of these patients had heart valves and 50% were on AC or had elevated coagulation measures. Furthermore, AC was above target in only one of these patients. In 69% re-hemorrhage occurred within 10 days of the initial event. No risk factors for hemorrhagic events were identifiable. Our data indicated that restarting AC 3 days after a hemorrhage may be the safest course of action in neurosurgical patients (class III evidence -- recommended option).

P-003

Survival and migration of adult neural stem cells following transplantation for focal cerebral ischemic injury

J Kelly (Calgary), J Wong (Calgary), S Weiss (Calgary)*

Background: Treatment options for individuals who have sustained injuries to the central nervous system are limited. New restorative techniques including neural stem cell transplantation offer potential for restoration of the circuitry and function of the central nervous system. Adult neural stem cells are one option for cell replacement therapy that avoids ethical issues associated with the use of embryonic or fetal stem cells. We report the successful transplantation, survival and migration of murine adult neural stem cells following focal cortical ischemic injury in rodents. *Methods:* Adult long-evans rats were subjected to focal cortical ischemic injury using the pial-stripping model. Murine adult neural stem cells from the subventricular zone were harvested and grown under neurosphere forming conditions. Cells were transplanted into the contralateral, uninjured hemisphere of lesioned animals seven days following injury. Immunohistochemical techniques were used to identify transplanted stem cells. *Results:* Murine adult neural stem cells from the subventricular zone survive up to four weeks and migrate when transplanted into the contralateral hemisphere of rodents following focal cerebral ischemic injury. *Conclusions:* Adult neural stem cells survive and migrate following transplantation and offer a potential source of cells for restorative therapy of the injured central nervous system.

P-004

Ruptured aneurysm at the choroidal branch of the posterior inferior cerebellar artery: a case report, review of the literature and proposed pathogenesis

Nancy McLaughlin (Montreal), Michel W. Bojanowski (Montreal)*

Background: Aneurysms rarely occur at the choroidal branch of the posterior inferior cerebellar artery (PICA). Their pathogenesis is not well-understood. *Method:* Case report and review of the literature *Results:* A 69-yr-old female was admitted for a sudden onset of severe headache with nausea and vomiting. Soon after arrival, she became less responsive. A head CT-scan revealed an intraventricular hemorrhage (IVH) predominantly in the 4th and 3rd ventricles with hydrocephalus and without subarachnoid hemorrhage. Cerebral angiography demonstrated an aneurysm at the choroidal branch of the PICA. The aneurysm was resected by a telovelotonsillar approach through a bilateral suboccipital craniotomy. The patient made a remarkable recovery. The literature describes 5 other cases of aneurysms arising from a choroidal branch of the PICA. Hypertension was a common finding. *Conclusion:* Aneurysms arising from a choroidal branch of the PICA are rare.

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Hypertensive vessel damage might be a major factor in their pathogenesis. We propose that the rupture of an hypertensive aneurysm might account for some isolated spontaneous IVH.

P-005

Thromboembolic complications after aneurysm coiling using adjunctive techniques

A Mitha (Calgary), W Hu (Calgary), M Hudon (Calgary), W Morrish (Calgary), J Wong (Calgary)*

Background: Endovascular coiling has recently afforded a minimally invasive means of effective aneurysm therapy. However, new technical adjuncts such as neck remodeling with balloons or stents for broad-necked aneurysms, and coated coils to improve treatment durability, have added layers of technical complexity and, presumably, risk to the procedure. We examined our recent experience of patients undergoing aneurysm coiling since the advent of these technologies to delineate the rate of thromboembolic complications associated with this procedure. *Methods:* We performed a retrospective chart review of aneurysms treated by coiling at a single tertiary care institution since July 2001. Outcomes of thromboembolic events were classified as asymptomatic, minor, or major. *Results:* 79 patients with 90 aneurysms were identified. 52% (47/90) of cases were acutely ruptured. Balloons were used in 29% (26/90), stents in 13% (12/90), and coated coils in 46% (41/90). Thromboembolic complications occurred in 21% (19/90) of patients. Clinically, these events were asymptomatic in 63% (12/19), minor in 11% (2/19), and major in 26% (5/19). Univariate testing showed no significant association between the overall use of balloons, stents, or coated coils with thromboembolism. *Conclusion:* Endovascular coiling is a reasonably safe method of aneurysm treatment and the use of adjunctive technologies does not add significantly to procedure risk.

P-006

Communicating hydrocephalus after endovascular coiling of an unruptured aneurysm

A Mitha (Calgary), W Hu (Calgary), J Wong (Calgary)*

Background: Although endovascular coiling is a relatively new therapy for intracranial aneurysms, most of the immediate or subacute intracranial complications have been recognized and well-documented. These complications include vessel dissection, hemorrhage, and thromboembolism leading to transient or permanent neurologic deficit. To our knowledge, hydrocephalus has never been reported as a complication of endovascular coiling of an unruptured aneurysm. *Methods:* We present a case of a 53 year old female who developed communicating hydrocephalus following endovascular coiling of an unruptured intracranial giant left posterior communicating artery aneurysm using 35 Hydrocoils. A literature search was performed to find documentation of similar cases and potential mechanisms are explored. *Results:* No cases of hydrocephalus following coiling of an unruptured aneurysm were found in the literature. Possible mechanisms for the development of communicating hydrocephalus in this patient may include the release of significant amounts of protein, either endogenous or from the coils themselves, into the subarachnoid space. *Conclusion:* Hydrocephalus as a complication of endovascular coiling of an unruptured intracranial aneurysm, as in the case presented, is an extremely rare, if ever, reported event. Nevertheless, its potential for development in the context of relatively new endovascular therapies and devices, should be recognized in similar patients who develop worrisome symptoms.

P-007

An aneurysm made angiographically occult by meningioma compression

K Petrecca (Montreal), D Sirhan (Montreal)*

Background: The association of intracranial aneurysms and brain tumors are rare although aneurysms have been reported in patients with a variety of brain tumors, the coincidence being highest with meningiomas. SAHs are secondary to aneurysm rupture in almost all cases. *Methods:* We present a case report and review the literature regarding coincident intracranial aneurysms and brain tumors. *Results:* We report here the case of an 84 year-old woman who presented with a history consistent with a ruptured ICA aneurysm made angiographically occult by an adjacent parasellar meningioma. *Conclusion:* To our knowledge this is the first example of an aneurysm made angiographically occult by brain tumor compression.

P-008

Angioplasty and stenting for symptomatic intracranial atherosclerosis

G Redekop (Vancouver), D Graeb (Vancouver), C Haw (Vancouver), R Heran (Vancouver)*

Background: Anticoagulation or antiplatelet therapy is the standard treatment for symptomatic intracranial atherosclerosis. Angioplasty and stenting is an emerging alternative for patients with refractory symptoms in spite of best medical therapy. *Methods:* Twenty-two patients with symptomatic intracranial atherosclerosis underwent angioplasty and stenting of twenty-four intracranial vessels. Lesions were in the internal carotid artery in 8 cases (33%), middle cerebral artery in 5 cases (21%), and vertebrobasilar circulation in 11 cases (46%). Five patients had simultaneous stenting of the ipsilateral extracranial carotid artery and one had stenting of the vertebral artery origin. *Results:* Stents were successfully deployed in twenty-three of the twenty-four vessels (96%). Vessel tortuosity precluded stent delivery in one case, and the procedure was limited to angioplasty alone, with dissection noted and symptomatic recurrent stenosis observed within 6 months. Two procedure-related strokes were observed (8%), due to the snowplow effect of perforating vessel occlusion. No in-stent stenosis or recurrent symptoms have been noted in follow-up in stented patients (mean = 6 months), although 1 had symptomatic progression of disease at another intracranial site. *Conclusions:* Percutaneous revascularization for intracranial atherosclerosis can be accomplished using current device technology with relatively low rates of morbidity. Our experience and that reported in the literature suggests that primary stenting is preferred over angioplasty alone due to the lower risk of dissection and recurrent stenosis.

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P-009

Physiologic and Pathologic Differences and Mortality in the Intracerebral Hemorrhage of the Anticoagulated Patient

M Shamji (Ottawa), B Benoit (Ottawa), E Fric (Ottawa), J Cole (Ottawa)*

Background: Oral anticoagulation reduces the risk of thromboembolic stroke but harbours the possibility and attendant mortality of intracerebral hemorrhage. Physiologic hypertension helps maintain cerebral perfusion, but may be deleterious in this patient population by promoting hematoma expansion. *Methods:* We retrospectively reviewed 265 consecutive patients with spontaneous intracerebral hemorrhage presenting to The Ottawa Hospital over three years. Among these 178 had consecutive CT scans permitting analysis of hematoma growth. Patients were stratified into "control", "anticoagulated", and "excessively anticoagulated" categories. *Results:* Higher mortality was noted in anticoagulated patients. This group experienced more likelihood of hematoma expansion and an elevated mean arterial pressure at presentation compared with the control group. No association was noted between anticoagulation and initial hematoma size or presenting level of consciousness. Supratherapeutic INR was additionally associated with predilection for posterior fossa hemorrhage, hematoma expansion, and higher mortality. *Conclusions:* Mortality was increased in anticoagulated patients despite similar hematoma size and location. The higher initial mean arterial pressure has not been previously described in this setting. This correlates with propensity of these hematomas to expand after initial imaging and may partially mediate the mortality effect. Early intervention to reverse anticoagulation and moderate blood pressure may help mitigate these deleterious effects.

P-010

Presentation of posterior fossa syndrome secondary to a post-operative thalamic hemorrhage

F Siddiqi (London), A. Ranger (London)*

Introduction: Posterior fossa syndrome (PFS) is a well recognized entity after cerebellar surgery in the pediatric population and is a combination of mutism and appendicular hypotonia which is reversible. The pathophysiology is controversial, and has implicated the vermis, the deep cerebellar nuclei, and the dento-thalamo-cortical pathway. *Case History:* A 3-year old male presented with a pilocytic astrocytoma involving the thalamus extending into the third ventricle. A gross total resection was achieved. Post-operatively, he had a deterioration in neurological function. He developed mutism and appendicular hypotonia. A CT demonstrated a thalamic hemorrhage with third ventricular extension. His symptoms gradually improved. *Discussion:* PFS has been described as a complication of cerebellar surgery. A recent case report of a child with a dorsal midbrain lesion causing mutism (J. Neurosurg. 2002 96(3): 607-10, Mar) as well as a child with post-operative mutism (J. Neurosurg. 1994 81 (1): 115-21) following operative injury to the supplementary motor area are examples of mutism which in combination with our case map out lesions along the dento-thalamo-cortical tract outside of the cerebellum. This suggests that disruption of this tract is the etiology of cerebellar mutism and PFS. No other cases of thalamic lesions leading to PFS exist in the literature to our knowledge.

Stroke

P-011

Giant cell arteritis and bilateral vertebral arteries occlusion/stenosis.

JM Boulanger (Calgary), T Watson (Calgary), C Sivakumar (Calgary), S Subramaniam (Calgary), J Roy (Calgary)*

Background: Although rare, bilateral vertebral artery occlusion/stenosis (BVAOS) has been described in association with giant cell arteritis (GCA). All cases had underlying classical symptoms of GCA. *Methods:* We report a case of BVAOS and GCA without any other features of GCA. *Results:* A 81 years old man presented with ataxia, dysarthria and right hemiparesis worsening over 12 hours. He denied any headache, fever, jaw claudication or constitutional symptoms. A CT scan revealed bilateral cerebellar and occipital acute ischemic changes. Vascular investigations (CT angiography, cerebral angiogram) showed an occlusion of the left vertebral artery and a severe stenosis of the right vertebral artery. The anterior circulation vasculature was unremarkable. Despite platelets inhibitors, the patient's condition deteriorated over two weeks. The erythrocyte sedimentation rate (66 mm/h) and the c reactive protein (51.1 mg/L) were markedly elevated. A temporal artery biopsy was performed and a diagnosis of GCA was made. Even though the patient received intravenous corticosteroids, he became quadriparetic and was transferred to a long term care facility. *Conclusions:* GCA can present as BVAOS without any other symptoms of GCA. Rapid diagnosis and treatment are mandatory. Inflammatory markers should be verified in symptomatic BVAOS, especially in elderly patients.

P-012

Stroke in patient with a documented DVT: searching for right to left shunt

MS Hussain (Edmonton), N Rizvi (Edmonton), S Al-Dandashi (Edmonton), M Saqqur (Edmonton), A Shuaib (Edmonton)*

Background: Venous to arterial thromboembolism is an uncommon but significant and often occult cause of stroke. Even when venous hypercoaguability is found, demonstrating a venous to arterial shunt can be difficult. *Methods:* Case Report/Literature review. *Case Presentation:* A 64-year-old woman with an unremarkable past medical history developed progressive swelling of her right leg over two week period. Two days before coming to hospital, she discovered that the sensation on the left side of her face was diminished, which was confirmed on physical exam. A Doppler ultrasound of the right leg confirmed the presence of a DVT. A CT scan of the head was performed and revealed a small infarct in the right corona radiata. Power-M-mode transcranial Doppler (PM-TCD) bedside ultrasound bubble study revealed positive microbubble signals (MBS) at rest and with Valsalva maneuver, indicating right to left shunt. Trans-esophageal echocardiography confirmed the presence of PFO. *Discussion:* PM-TCD is a useful bedside tool to assess stroke patients for right to left shunts. All stroke patients with suspected or confirmed venous thromboembolism should undergo PMD-TCD PFO bubble study to help guide the need for further investigations and treatment.

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P-013

The impact of chronic renal failure on cerebrovascular disease.

G Jickling (Halifax), G Gubitz (Halifax), C Constantine (Halifax), SJ Phillips (Halifax)*

Background: Cardiovascular disease, including cerebrovascular disease is common in patients with renal failure. In coronary artery disease, chronic renal failure has been identified as an independent risk factor. Whether such a relation exists for cerebrovascular disease is less clear. *Methods:* A systematic review of medical literature on cerebrovascular disease and chronic renal failure was performed using the Pubmed database. In total, 143 articles were identified for review. *Results:* Stroke risk in renal failure is reported to be 4-10 fold that of the general population. The increased risk is explained in part by a higher prevalence of traditional vascular risk factors. Other non-traditional factors may confer additional risk. These include anemia, increased inflammation, increased oxidative-stress, malnutrition, hypoalbuminemia, calcium-phosphate dysequilibrium, and hyperhomocystemia. Whether such factors are causal or markers of accelerated vascular disease remains unclear. Evidence exists to support an increased frequency of all ischemic stroke subtypes in renal failure patients. Few data are available regarding outcomes and treatment of patients with cerebrovascular disease and renal failure. *Conclusion:* The burden of renal failure and cerebrovascular disease is predicted to increase as our population ages. Further research is required to understand the role of renal failure as a risk factor in cerebrovascular disease.

P-014

Arterial reocclusion and recurrent stroke following thrombolysis; correlation of clinical outcomes to transcranial Doppler ultrasonography and CT perfusion scan findings.

A.Y. Jin (Kingston), D.G. Brunet (Kingston), O. Islam (Kingston), F.W. Saunders (Kingston)*

Background: The clinical impact of late arterial reocclusion and recurrent stroke during the first five days following thrombolysis was studied. *Methods:* All patients with a middle cerebral artery stroke presentation had a non-contrast CT scan. Transcranial Doppler (TCD) examinations of the anterior circulation were performed during the initial admission and daily over the first five days of hospital admission. CT and CT perfusion scans were done on day 5. NIHSS scores on admission and days 1 to 5 and the modified Rankin Scale (mRS) score at three months were obtained. *Results:* Thirteen patients were enrolled in this ongoing study. Three out of thirteen (23%) patients demonstrated arterial reocclusion and/or a new infarction. Two patients demonstrated late arterial reocclusion on TCD; one of these patients also demonstrated new bilateral cerebellar infarctions on CT. A third patient showed a new right cerebellar infarction. These patients had a poor clinical outcome as reflected in the NIHSS score on day 5. Follow-up clinical assessments are ongoing. *Conclusions:* Arterial reocclusion and recurrent stroke during the first five days after thrombolysis occurs in a significant number of patients and is associated with a poor clinical outcome on day 5.

P-015

Reversible segmental cerebral vasoconstriction (Call-Fleming syndrome) in a child.

A Kirton (Calgary), J Diggle (Calgary), W Hu (Calgary), E Wirrell (Calgary)*

Background: Reversible segmental cerebral vasoconstriction (RSCV) consists of symptomatic vasospasm ranging from isolated thunderclap headache to focal neurological deficits secondary to ischemia or infarction. *Methods:* Case Report. *Results:* A healthy 13 year-old boy experienced the sudden onset of a severe, diffuse headache upon surfacing from a deep dive in a swimming pool. Severity was maximal at the onset and improved over several hours. The same headache recurred three times over the next four days and a low baseline headache persisted throughout. Vomiting occurred once and mild photo/osmophobia were reported but throbbing, aura, or autonomic symptoms were absent. Focal neurological signs or symptoms were absent and he denied previous history of headaches, medications, drugs, or trauma. Two normal CT scans were performed within hours of separate headaches. CSF study on day 5 was bloody with no xanthochromia. MRI/MRA/MRV of the brain and vasculitic work-up were normal. Cerebral angiography on day 6 demonstrated smooth narrowing of multiple proximal cerebral vessels including supraclinoid ICA, M1, and A1 on the right and M1 on the left with no vascular malformations. By ten days, the patient's headaches had resolved and repeat angiography was normal. *Conclusion:* RSCV should be considered in a child with thunderclap headache.

P-016

Wallenberg syndrome from a vertebral artery dissection: 25 years later.

G. Lapointe (Quebec), S. Verreault (Quebec), J-L. Gariépy (Quebec), J-P. Bouchard (Quebec)*

Objective: To review the long term evolution of Wallenberg syndrome and the results of the recent investigation of one case first seen in 1978. *Case report:* A 42 year old man was suddendly struck at work by vertigo, vomitting and shift to the left. On admission, he was somnolent, dysphonic and severely dysphagic. On discharge were noted: left Horner syndrome, rotatory nystagmus, trigeminal hypodysesthesias, stance shift and limb incoordination; right limb dysesthesias. Dysphagia improved rapidly, but the syndrome has remained virtually unchanged. He has never resumed his work. Recently the patient complained of left trigeminal neuralgia. Results: A "modern" investigation was completed, including cervical Doppler, CT angiography and MRI. The neck vessels were normal, except for a left vertebral artery thrombosis and no PICA visualization. A large infarct of the left lateral and posterior medulla and most of the cerebellar hemisphere was manifest. No metabolic risk factor was identified but the patient was heterozygous for the C677T mutation of the M.T.H.F.R. gene. *Conclusions:* Long term disability is frequent in Wallenberg syndrome. Central poststroke pain occurs in 1/4 of the cases. Trigeminal neuralgia was rarely reported as a late sequela.

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P-017

Reference values for breath holding index in evaluation of vasomotor reactivity by transcranial doppler sonography

*Sayed Ali Mousavi * (Isfahan), Bahador Asadi (Isfahan), Fariborz Khorvash (Isfahan)*

Background: The assessment of cerebral vasoreactivity can provide information regarding the reserve capacity of cerebral circulation. Reduction of this property has been found in association with situations predisposing toward cerebrovascular disease. In this study, we defined vasoreactivity of brain vessels according to age and sex of the patients. *Material and Methods:* In this descriptive study 289 healthy subjects (without hypertension, diabetes mellitus, obesity, smoking, CHF, CHD) were admitted from Jan. 2004 to June 2004. The population according to age and sex were divided to four groups (women and men more and less than 30). After determination of each patient's flow velocity of MCA by means of a transcranial doppler instrument, before and after 30s apnea, breath holding index was calculated. Data was analyzed by SPSS/win usnig. *Results:* BHI was comparable in women and men (0.918±0.40 versus 0.637±0.22). In fact, considering woman and men together BHI was significantly lower in older (age > 30) women (0.812±0.31) than in younger (<30 years) women (0.995±0.44; P<0. 001) but there was no significant deference between older (age > 30) men (0.62±0.23) and younger (<30 years) men (0.65±0.20; P > 0. 05). *Conclusions:* The average of BHI was lower in men than in women in total and in all age subgroups. BHI was relatively constant in all age subgroups in men but there was significant decline in BHI by increasing age in women. So despite many physiologic changes related to aging vasomotor reactivity remains relatively constant in men but decreases in women. Findings of our study suggest that changes of cerebrovascular vasomotor reactivity in healthy subjects may be related to aging, but they are probably mainly influenced by sex.

P-018

Intracranial vessel occlusion in minor stroke deficits: Does it influence treatment decisions?

J Roy (Calgary), C Sivakumar (Calgary), S Subramaniam (Calgary), V Palumbo (Calgary), A Krol (Calgary), M Hill (Calgary), M Eliasziw (Calgary), A Demchuk (Calgary)*

Background: It is unclear if intracranial vessel occlusion (IVO) represents a target population for reperfusion in minor strokes. We examined the relationship of IVO (by CTA) on clinical outcome in minor stroke/ transient ischemic attack (TIA). *Methods:* We retrospectively studied patients with minor stroke (baseline National Institute of Health Stroke Scale [NIHSS] <= 6) or TIA who had a CTA of Circle of Willis completed. A good outcome was defined as a follow up mRS <2 anytime from discharge to 3-month (and/or when discharged to home) and a poor outcome as mRS>2 and/or discharge to rehabilitation or death. *Results:* 146 patients included, male 59%, mean age 63.1 years (SD 15.9), 36% TIA. Median baseline NIHSS was 2 (0-6) and pre-morbid mRS was 0 (0-3). Fifteen (10.2%) patients had vessel occlusion; 9(60%) in the anterior circulation. Ten patients (66%) with occlusion had good outcome. In patients without occlusion (n=131), 104 (79%) had good outcome. Patients without occlusion are 1.2 times more likely to have a good outcome compared to patients with occlusion (95% CI: 0.8 to 1.7, p-value= 0.32). *Conclusion:* IVO detected by CTA in minor stroke/TIA does not predict a poor outcome. Role of recanalization strategies remains unclear in this population.

P-019

Basal skull fracture masquerading as anterior inferior cerebellar artery (AICA) stroke

S Subramaniam (Calgary), C Sivakumar (Calgary), J Roy (Calgary), JM Boulanger (Calgary), V Palumbo (Calgary), M Hill (Calgary), T Watson (Calgary)*

Background: Stroke "mimics" are nonvascular disease processes presenting with a stroke like clinical picture and often poses a diagnostic challenge in the emergency room. Skull fractures can sometimes present with stroke like symptoms and can be easily missed, especially if one looks only at the brain parenchyma and not the bone. *Methods:* We present a case of basal skull fracture presenting as Anterior Inferior Cerebellar Artery Stroke syndrome. *Results:* 48 year old male presented to the emergency room after a fall from an inebriated state. He complained of sudden onset dizziness, vertigo, and unsteadiness in his legs. Neurological exam revealed dysarthria, right facial weakness, right sensorineuronal hearing loss and ataxia. CT scan of the brain revealed normal parenchyma, but the bone windows revealed left basal skull fracture with minor displacement. Magnetic resonance imaging of the brain and neck revealed normal parenchyma and vessels. The patient was seen by the neurosurgeons and sent home on conservative management. *Conclusions:* Basal skull fracture is an unusual presentation of anterior inferior cerebellar stroke. The bone fragments impinge on the cranial nerves, adjacent brain parenchyma and can mimic anterior inferior cerebellar stroke. With novel emerging therapies for acute stroke, the diagnosis of ischemic stroke and stroke "mimics" is an area of continuing concern.

P-020

Jaw claudication resulting from cardioembolic occlusion of the external carotid artery

D Toffoli (Montreal), M Dominguez (Montreal), S Élysée (Montreal), S Lanthier (Montreal)*

Background: Primary artery diseases affecting the external carotid artery (ECA) typically cause ischemia of masticatory muscles and jaw claudication (JC). *Methods:* Case report and literature review of cardioembolic occlusion of the ECA as a cause of JC. *Results:* A 77 year-old man with atrial fibrillation (AF) experienced right-sided jaw pain upon mastication and left-sided weakness 7 hours later. He denied recurrent jaw pain, headaches, vision loss, diplopia, fever, asthenia, weight loss, and symptoms of polymyalgia rheumatica. Physical examination showed left-sided sensorimotor deficit and homonymous hemianopia, irregular cardiac rhythm, and unremarkable carotid and temporal arteries. Brain CT revealed a right middle cerebral artery infarct. EKG confirmed AF. Echocardiography identified no atrial thrombus. INR was 1.4. Erythrocyte sedimentation rate, fibrinogen level, haemoglobin level, and aPTT were normal. Duplex ultrasonography showed 0-20%

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bilateral internal carotid artery stenoses, normal left ECA, and occluded right ECA. Eight weeks later, repeat duplex ultrasonography showed normal right ECA. We found no published reports of cardioembolic JC. *Conclusions:* In the current case, the absence of inflammation markers, briefness of JC suggesting rapid collateralization of the occluded ECA, subsequent cardioembolic stroke, and normalization of the right ECA at 8 weeks support cardioembolic ECA occlusion as a cause of JC.

P-021

Cerebrovascular Disease in Progeria

C Waisburg (Vancouver), M Nilsson (Vancouver), K Poskitt (Vancouver), R Heran (Vancouver), P Teal (Vancouver), M Connolly (Vancouver)*

Background: Hutchinson-Gilford Progeria Syndrome (HGPS) is an extremely rare progressive disorder characterized by premature and accelerated aging and early growth failure. It is associated with early atherosclerosis involving coronary and cerebral vasculature, which results in significant morbidity and mortality. The objective is to describe angiographic findings and cerebral perfusion pattern in a child with HGPS and recurrent transient ischemic attacks and stroke. *Methods:* Retrospective review of the medical records. *Results:* A ten-year-old boy with HGPS and mild hypertension presented with an episode of transient right sided paresthesiae, hemiparesis and dysphasia. In retrospect, he had prior transient episodes of right hemisensory symptoms. No focal neurological findings were observed on initial examination. He had bilateral carotid bruits. CT head scan revealed multiple areas of cerebral infarction of varying ages. Cerebral angiography demonstrated 99% stenosis of the left internal carotid artery, 80% stenosis of the right internal carotid artery, >90% stenosis of the left vertebral and absent right vertebral artery. There were multiple collateral vessels emanating from the external carotids, occipital and posterior temporal arteries. The left hemisphere was supplied via the basilar artery. Xenon CT revealed cerebral blood flow of 18-35ml/100gram/minute with no reserve following acetazolamide (20mg/kg) in the left hemisphere but there was vasodilation in the right hemisphere. Coronary angiography was normal. *Conclusion:* Extreme narrowing of cerebral vessels and reduced regional cerebral blood flow may be observed in HGPS.

EPILEPSY, EEG, NEUROPHYSIOLOGY

P-022

The direct cost of epilepsy at a tertiary care Canadian hospital

SN Ahmed (Edmonton), K Heck (Edmonton), J Soderstrom (Edmonton), H Lari (Edmonton), B Rowe (Edmonton)*

Background: Epilepsy is a common neurological condition affecting approximately 200,000 Canadians. Through this project we sought to address the direct cost of epilepsy at the University of Alberta Hospital. We hoped to use this information in optimizing resource allocation and improving support system. *Methods:* A 4-year retrospective study was conducted at the University of Alberta Hospital. The study included all patients with epilepsy presenting to the emergency room. 197 out of 380 randomly selected patients qualified for the study. The direct cost of epilepsy care was based on the ambulance use, hospital fee, consultation fee, diagnostic procedures and laboratory investigations. The Capital Health Authority and the Alberta Ambulance Billing Department provided cost data. Consultation cost was based on the billing rates by Alberta Health. *Results:* The total cost averaged to $866.30 per patient. Based on an estimate of the total sample this amounted to approximately $407,000 per year. The major portion of the cost was related to the hospitalized patients. *Conclusion:* Epilepsy incurs a significant cost to the health care system. A major portion of this cost is related to the hospitalized patients. A close follow-up with a structured support system can potentially minimize cost and optimize delivery of a quality care.

P-023

What do nurses and physicians think about the need for specific dietary restrictions in patients with epilepsy?

AliAkbar Asadi-Pooya (Shiraz), Ahmad Hossein-Zade (Shiraz)*

Background: Avicenna the great Iranian scientist 1000 years ago recommended that epileptic patients should avoid certain foods. In this study, we attempted to identify beliefs and experiences of the nurses and physicians about the need for specific dietary restrictions in epileptic patients. *Methods:* A cross-sectional study was carried out using a questionnaire in Shiraz, Iran, in 2004. Nurses from pediatric and internal medicine wards of Nemazee and Dastghaib hospitals and also general practitioners, pediatricians and internists were included in the study. *Results:* The total number of participants was 250. Totally, 58.4% of the participants believed in the relation between specific food consumption and the occurrence of seizure. Personal experiences for the occurrence of seizure after specific food consumption were reported by 28% of the participants. Dairy products, sour foods and food additives were the most common responsible foods reported. *Conclusion:* Clearly, participants usually wished to know if their epileptic patients need any dietary restrictions. It is invaluable to take the experiences of health care workers caring for an epileptic patient into consideration and evaluate the relation between specific food consumption and seizure. This relation may have various possible causes such as food and the disease interaction or food and drug interaction.

P-024

Surgical cure of a child with intractable orbital frontal epilepsy: A Case Report

A Attar (London), R McLachlan (London)*

Background: Little is known about rare seizures originating from the orbital-frontal (OF) region. Due to the connections within the limbic system, OF seizures can be confused with temporal lobe seizures. *Methods:* Case report of an 8-year-old child with intractable epilepsy of OF origin. *Results:* An 8 year-old boy had intractable epilepsy of four years duration. He was previously healthy and had no pertinent antecedents. Seizures were stereotyped, starting with a cephalic sensation associated with a bad feeling in the stomach. Later, loss of awareness occurred along with oroalimentary automatisms, staring and tonic extension of the arms followed by postictal drowsiness and lethargy lasting about a minute. No grand mal seizures. Medical and neurological examination was normal.

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Scalp interictal EEG showed prominent apparent right temporal abnormalities and diffusely in the right hemisphere. No definite electrographic change was noted on ictal scalp recording. However, subdural electrode ictal recording consistently showed right OF seizure onset. Brain MRI was normal. Removal of the right OF cortex rendered the patient seizure-free for over 17 years on no medications. Pathology revealed a neuronal migration disorder. *Conclusions:* We report a child cured of OF epilepsy by surgery. EEG telemetry with intracranial recording is required to differentiate OF epilepsy from temporal lobe epilepsy.

P-025

Determination of frequency of some causes of seizure recurrence in fifty patients suffered from seizure

Parviz Bahrami (Khorramabad), Shareyar Fatehi (Khorramabad), Mohammad Javad Tarahi (Korramabad)*

Background: The key to management of seizure is to develop a clear, simple, and stepwise approach to the initial history, physical exam, and treatment, with an emphasis on not missing the most common and often easily treatable causes of seizure activity. *Method:* The main aim of this prospective descriptive study is determination of some causes of seizure recurrence frequency in patients suffering from epilepsywho were followed up in Lorestan University of Medical Sciences during a period of six months in 2001. Among some variables that were evaluated 5 variables such as: type of seizure, continues use of drugs, central nervous disease, and appropriateness between type of seizure with medication and resistance nature of seizure with medication have a special importance for this study. *Result:* 1) 58% of patients had a generalized seizure, 34% a focal and 8% secondary generalized seizure. 2) 58% of recurrence has occurred due to withdrawal of drug. 3) 22% of patients had a central nervous system disease. 4) 16% of cases have shown a resistance between natures of seizure type with medication 5) 4% of patient has not appropriateness between types of seizure with medication. *Conclusion:* it is necessary to explain to patients about importance of recurrence of seizure, continued use of drug and gradual withdrawal of drug only by physician request. Diagnosis of type of seizure and use of drug of choice is also important for control of seizure. For drug resistance seizure, investigation to undergo surgical treatment is indicated.

P-026

Assessing the quality and contents of Canadian e-Health web sites for patients with epilepsy

JG Burneo (London)*

Background: Despite the substantial amount of epilepsy-related information available on the internet, little is known about its quality. Epilepsy-related information in english on the Canadian internet was reviewed. *Methods:* Popular search engines (google.ca, yahoo.ca, ca.altavista.com, simpatico.msn.ca) were interrogated. Websites primarily aimed at patient and family education, geared toward human epilepsy, and epilepsy in general as opposed to one specific type or aspect of epilepsy, were included. Websites then were subdivided in proprietary (directly sponsored by industry) and non-proprietary, and evaluated according to compliance with the principles of the Health-on-the-Net (HON) Foundation-Code-of-Conduct. Web sites without comprehensive contents were excluded. Comparison between total scores was done using Rank Test. Categorized descriptors were assessed by t-tests. *Results:* 5 proprietary and 14 nonproprietary websites were identified. None of them were compliant with all 8 principles of the HON code. The average number of principles with which these sites were in compliance was 3.3 (range: 1-6.5, p=0.4, proprietary vs. non-proprietary). Compliance with each principle was assessed and results will be presented. *Conclusions:* The internet has the potential to be a very powerful educational tool for patients with epilepsy. However, many easily accessed epilepsy web sites do not comply with accepted standards for health web sites.

P-027

Morbidity associated with intracranial placement of electrodes for epilepsy surgery evaluation

JG Burneo (London) , D Steven (London) , A Parrent (London)*

Background: The performance of invasive monitoring for investigation of medically intractable epilepsy may be associated with undesirable morbidity. We evaluate the presence of these possible complications analyzing our experience. *Methods:* We did a retrospective review of the clinical charts from the patients invasively evaluated for epilepsy surgery between 2000 and 2004, at the London Health Sciences Centre, creating a database of their clinical information. *Results:* 116 patients (57 males, 59 females) with a mean age of 32 years (range: 9-65), underwent intracranial placement of electrodes for epilepsy surgery investigation. A mean of 8 strips (range: 1-17) were placed in 115 patients. 11 patients had grids and 5 depth electrodes. 37 patients received unilateral coverage while 79 bilateral. Frontal lobe was covered in 78, temporal in 93, parietal in 24, and occipital in 27 patients. Average duration of investigation was 12.3 days (range 3-29). Evaluation allowed the performance of surgical resection in 85 patients. Complications were seen in 9 patients, characterized by infection, intracranial hemorrhage, pneumocephalus, aseptic meningitis, transient neurological deficits, status epilepticus, and confusion. *Conclusions:* Complication rate is low and our findings disagree with published literature on this topic. We discuss possible predictive factors and ways to avoid complications.

P-028

Surgical cure of temporal lobe seizures with automatism and amnesia - a 50-year follow-up.

*William Feindel** (Montreal)*

Background: Stimulation of the periamygdaloid region during surgery can produce auras, automatism and amnesia that characterize epileptic attacks originating in the mesial temporal lobe (Feindel, Penfield and Jasper, 1952; Feindel and Penfield, 1954). That evidence coupled with the hypothesis of "incisural sclerosis" predicating damage to mesial temporal tissue from tentorial herniation (Earle, Baldwin and Penfield, 1953) led to the procedure of anteromesial temporal lobe excision (Penfield and Baldwin, 1953). This report highlights advances during the past five decades in this effective surgical procedure. *Method:* Reports in the early 1950s from several centres where surgical treatment of temporal lobe seizures was being developed have been critically reviewed.

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Advances since then include improved EEG monitoring, advent of brain imaging for preoperative diagnosis and postoperative monitoring, reduction in size of the focal surgical excision and improvment in surgical technique. *Results:* Many neurosurgical centres report postoperative arrest of seizures in 70 percent or more of patients, depending on the rigor of diagnostic selection, type and location of the intrinsic pathology and, not least, the experience and skill of the surgical and nursing team. High resolution imaging studies show volumetric changes in the hippocampus but also in the amygdala and entorhinal cortex. *Conclusions:* Future goals of surgery for temporal lobe seizures should aim at achieving minimal excision of epileptogenic tissue in the mesial temporal region consistent with arrest of seizures and minimal cognitive deficits.

P-029

Increased High Frequency Oscillations Precede in vitro Low Mg2+ Seizures

H Khosravani (Calgary), R Pinnegar (Calgary), R Mitchell (Calgary), B Bardakjian (Toronto), P Carlen (Toronto), P Federico (Calgary)*

Background: High frequency oscillations (HFOs) in the range of 80 Hz and above have been recorded in neocortical and hippocampal brain structures in vitro and in vivo, and have been associated with physiological and epileptiform neuronal population activity. Frequencies in the fast ripple range (> 200 Hz) are believed to be exclusive to epileptiform activity and have been recorded in vitro, in vivo, and in epileptic patients. Although the presence of HFOs is well characterized, their temporal evolution in the context of transition to seizure activity is not well understood. *Methods:* Using an in vitro low magnesium model of spontaneous seizures, we obtained extracellular field recordings (hippocampal regions CA1 and CA3) of interictal activity during the transition to seizure-like events. Interictal and ictal recordings were analyzed for power spectral composition, in time, using a local multi-scale Fourier transform. The power spectrum of interictal and ictal discharges was quantified into four frequency bands spanning sub-ripple, ripple, and two fast ripple frequencies. *Results:* A statistically significant increasing trend was observed in the amplitude of ripple (100-200 Hz) and fast ripple (200-300 Hz) activity leading to the start of seizures. *Conclusions:* Temporal patterns of HFOs during epileptiform activity are indicative of dynamic changes in synchronization in neuronal networks and their characterization may offer insights into pathophysiological processes underlying seizure initiation.

P-030

Therapy of Gelastic Seizures (GSs) in Multiple Sclerosis (MS)

D. Kountouris (Athens)*

Background: Approximately 5% of the MS patients are affected by epileptic seizures. In several of them they manifest as gelastic seizures. We investigated the existing therapeutic effects in MS. *Methods-Materials:* We observed the follow-up of 5 MS patients (3 male, 2 female) with GS for about 5 years. Within this time we recorded all treatments they had received as well as all results of the neuroradiologic and neurophysiologic examinations, collected and evaluated them. *Results:* In only 2 of the patients, there was a demyelinisation lesion in cerebral MRI close to hypothalamus without direct contact, though. None of them presented a hamartoma. On the contrary, the electroencephalograph (EEG) confirmed in all patients multifocal epileptoform activity, mainly fronto-temporal. The only effective treatment was the administration of antiepileptic drugs with Mitoxantrone. *Conclusion:* The cause for GSs in MS must not be always a hypothalamic hamartoma. It is probably due to the autoimmune character of the disease. The most satisfactory treatment, therefore, is Mitoxantrone with antiepileptic drugs.

P-031

Vagus nerve stimulation for epilepsy: the Quebec City experience.

S Larue (Quebec), R Desbiens (Quebec), D Lacerte (Quebec), H Brochu (Quebec), C Picard (Quebec)*

Background: Vagus nerve stimulation (VNS) is an accepted treatment option for refractory epilepsy. Pivotal studies demonstrated that up to 50% of implanted patients had a 50% seizure reduction. We assessed our local experience with this technique and compared it with the existing literature. *Methods:* Between 1998 and 2004, 18 patients were selected for VNS based on the severity of their epilepsy. In this retrospective study, data on demographics, seizure frequency before surgery and at last follow-up, average length of follow-up, side-effects and tolerability were collected. *Results:* The mean age of our patients was 27 years. The average follow-up was 24.4 months. 78% (14 of 18) of our patients improved (13 had their seizure counts improved by more than 50% [p=0,0011]). Three (16%) were unchanged and 1 patient (5%) reported deterioration. Complications were wound infection and ipsilateral vocal cord paralysis in one patient and transient tachycardia in another. *Conclusions:* VNS is well tolerated and effective for the treatment of refractory epilepsy. Its efficacy is sustained and comparable or better than the efficacy of new AEDs in our study population. The procedure was well tolerated by most.

P-032

Chronic hippocampal stimulation in temporal lobe epilepsy

R McLachlan (London), J Tellez-Zenteno (London), S Wiebe (Calgary), A Parrent (London)*

Background: There have been various attempts at electrical brain stimulation for the treatment of epilepsy but hippocampal stimulation has not been assessed systematically. *Methods:* Continuous stimulation (185hz, 90ms, 1.4-4.5v) was applied unilaterally through a four lead electrode stereotaxically inserted along the axis of the hippocampus in four patients with intractable partial seizures who were not candidates for temporal lobectomy because of the risk of memory deterioration. A randomized blinded n of 1 trial format was followed for 6 months with stimulation on or off during alternate months. *Results:* Seizure reduction compared to baseline was 100%, 50%, 30% and 0% in each patient. However no significant difference (T test, 95% CI) occurred between periods of on or off stimulation. Three subjects felt subjective improvement of more than 50% but quality of life assessed using QOLIE-89 did not

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change. No memory change or other complications occurred. *Conclusion:* These preliminary data support hippocampal stimulation as a potential new treatment for temporal lobe epilepsy. The most beneficial stimulation paradigms have yet to be determined.

P-033

A review of epilepsy in infancy at the Childrens Hospital of Eastern Ontario (CHEO)

R Melbourne Chambers (Ottawa), D Keene (Ottawa)*

Rationale: The incidence of epilepsy in childhood is highest during the first year of life. The outcome seems to be poor. This study aimed to determine factors which correlate with outcome in infantile epilepsy. *Methods:* At CHEO, the clinical, laboratory, electroencephalogram (EEG) and neuroimaging findings of infants, age 1 to 12 months presenting with epilepsy between January 1994 and September 2004 were retrospectively reviewed. *Results:* 25 patients (10 female, 15 male) were identified. The mean age at onset was 5 months. Development was initially normal in 20. The EEG showed an abnormal background in 10 patients and epileptiform activity in 16. Outcome: 13 patients had intractable epilepsy. 5 patients experienced seizure freedom for 12 months or longer. Developmental slowing occurred. The impact on language was most significant with 20 patients manifesting developmental delay. Abnormal developmental outcome was associated with abnormal background and epileptiform features on initial EEG and treatment with more than 3 anticonvulsants. Treatment with more than 3 anticonvulsants was associated with seizure intractability. *Conclusion:* Epilepsy in infancy is associated with a moderate risk of developmental delay and seizure intractability. EEG abnormalities and failure to respond to three anticonvulsants are associated with abnormal development.

P-034

Surgery in children with medically refractory temporal lobe epilepsy related to low-grade tumors

S Mittal (Montreal), JL Montes (Montreal), J-P Farmer (Montreal), B Rosenblatt (Montreal), F Dubeau (Montreal), F Andermann (Montreal), N Poulin (Montreal), A Olivier (Montreal)*

Background: Surgery has become an accepted treatment modality for carefully selected patients with focal epilepsy. The goal of this study was to describe the clinical and surgical aspects of a group of pediatric patients suffering from intractable epilepsy related to neoplasms in the temporal lobe. *Methods:* Etiologic, pathologic, and clinical features of possible prognostic significance were studied in 38 children who underwent temporal lobe surgery at the Montreal Neurological Institute and the Montreal Children's Hospital between 1985 and 2000. *Results:* The mean age of seizure onset was 6.5 years with duration of epilepsy ranging from 0.1 to 15.3 years. Preoperative MRI identified a mass lesion in all patients. Mean age at surgery was 11.3 years. Surgical approaches included: anterior temporal resection with lesionectomy in 16 patients (42%); lesionectomy alone in 11 children (29%); anterior temporal resection alone in 6 (16%); and transcortical selective amygdalo-hippocampectomy with lesionectomy in the remaining 5 patients (13%). Histopathological analysis revealed ganglioglioma in 21 patients, DNET in 5, astrocytoma in 5, oligodendroglioma in 3, mixed oligo-astrocytoma in 2, choroid plexus papilloma in 1, and pilocytic xanthoastrocytoma in 1. Thirty-six patients (94.7%) remained seizure-free at a mean follow-up of 12.1 years (range, 4.4 to 19.8). *Conclusions:* Our experience indicates that successful postsurgical outcomes with lesion-related epilepsies can be obtained in pediatric patients with minimal complications.

P-035

Juvenile myoclonic epilepsy: an under-recognized epilepsy syndrome

S Ryan (Halifax), M Sadler (Halifax), S Rahey (Halifax)*

Background: Juvenile myoclonic epilepsy (JME) is a primary generalized epilepsy syndrome preferentially responsive to valproic acid (VPA) compared to older anti-epileptic drugs (AEDs). Observations in an adult tertiary care epilepsy outpatient clinic prompted a review of the local experience with JME in the following domains: (a) diagnostic delay (DD), (b) reasons for diagnostic delay, (c) consequences of DD. *Methods:* JME patients were identified with a computerized database and hand search of outpatient clinic charts. DD was defined as the interval from first MD visit after onset of myoclonic jerks to diagnosis of JME. Other data collection included time to treatment with VPA, the number of previous consulting neurologists, possible reasons for DD, and adverse outcomes associated with DD. *Results:* Patients with JME = 61. Median DD = 6 years (mean = 9.6 years); mean time to treatment with VPA = 8.8 years. 32/42 patients not diagnosed with JME prior to evaluation in Epilepsy Clinic had seen at least 1 neurologist. The most common identified reason for DD was a failure to appreciate the presence/significance of myoclonus. Consequences associated with DD and suboptimum therapy will be shown. *Conclusion:* JME is under-recognized among community physicians, including neurologists, with important negative consequences for patient care.

P-036

Nonconvulsive Status Epilepticus in Pediatric Intensive Care Unit

M Saengpattrachai (Toronto), A Hunjan (Toronto), MA Cortez (Toronto), OC Snead III (Toronto)*

Background: Nonconvulsive status epilepticus (NCSE) is a frequently missed diagnosis in patients with altered consciousness. *Methods:* A retrospective review was done of all pediatric patients with an unexplained decrease in level of consciousness, no overt seizure activity and EEG recording performed within the 24 hours period, admitted or transferred to the Pediatric ICU, from January 2000 to December 2003. *Results:* There were 141 out of 311 cases (male/female ratio 1.9:1; mean age = 40.1 months, range 1 to 204 months). NCSE was detected in 16.3% (n=23). In these cases, some were previously healthy (43%) or with a history of seizure disorders (35%) before the diagnosis of NCSE was made (acute structural brain lesion 48%, acute non-structural brain lesion (17%) epilepsy-related seizure (13%), and others (22%). Right-sided epileptiform discharges (47.8%), left-sided (26.1%), and bilateral (26.1%); temporal region (23%) and frontal (18%). EEG's with slow

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frequencies in 56.5% and low amplitudes in 47.8%. Abnormal brain imaging was found in 78.2%, and cerebral infarction in 26.1%. Abnormal brain imaging with abnormal EEG was correlated in seven cases (30.4%). *Conclusions:* The prevalence of NCSE in the PICU is 16.3%. Early diagnosis of unexplained decrease in level of consciousness is warranted. NCSE impaired the patient's health significantly and it was often a treatable condition. Most patients were healthy and had no previous history of epilepsy.

P-037

An unusual electroencephalographic response to photic stimulation.

M Shapiro (Saskatoon), N Lowry (Saskatoon)*

Background: Classic photic electroencephalographic responses include photic driving, the photomyoclonic response, and the photoparoxysmal response. A 24-year-old female, with a syncopal event, had an unusual response to photic stimulation on electroencephalography (EEG). The response occurred repeatedly 0.5 seconds following photic stimulation. It was most prominent in leads F3-C3, F4-C4, and Fz-Cz. A prominent photic driving response was also seen. The patient had a normal neurological exam with the exception of decreased acuity in her right eye secondary to a refractive error. *Methods:* EEG was repeated with eyes open and eyes closed during photic stimulation. Visual, somatosensory, and brainstem auditory evoked responses were recorded. *Results:* This unusual photic response was reproducible on two separate occasions, 3 months apart. It was present at all frequencies from 3 to 30 Hz. *Conclusions:* This EEG finding likely represents a late component of the visual evoked response. It has not been previously well described in standard EEG texts. While it may represent an incidental finding in a single patient, it may be found to be more common if looked for specifically.

P-038

Myasthenia gravis and epilepsy: effect of plasma exchange on carbamazepine levels

Z Siddiqi (Edmonton), A Holt (Edmonton), S Ahmed (Edmonton)*

Introduction: Patient taking anti-epileptic drugs (AED) may require plasma exchange (PEX) for the treatment of an unrelated medical condition. Previous studies on the effect of PEX on AED levels are scarce with no existing guidelines to manage their dosage during PEX. *Methods:* We studied the total blood levels of Carbamazepine (CBZ) serially, before and after each PEX cycle, in an epilepsy patient who underwent PEX for treatment of myasthenia gravis. *Results:* The total blood CBZ levels remained within the therapeutic range throughout the course of PEX and no dose adjustment was required. A small but consistent reduction in the CBZ levels was noted immediately after each cycle, though overall, there was a gradual and cumulative increase in the blood levels over the duration of PEX. *Conclusion:* The total blood levels of CBZ are slightly affected by PEX, likely due to removal of the drug and redistribution among various body compartments. These alterations in the CBZ levels, however, do not appear to be clinically significant to merit adjustment of the CBZ dose during PEX.

P-039

Epilepsia partialis continua ipsilateral to a frontal focus

B Young (London), W Blume (London)*

Background: Lateralized clonic jerks of the extremities during epileptic seizures usually arise from epileptiform activity in the contralateral Rolandic cortex. We report a case in which one-sided extremity twitches related to epileptiform activity in the ipsilateral frontal lobe. *Report:* A 41 year old man had a ruptured right posterior communicating aneurysm that was complicated by post-operative vasospasm resulting in infarction in the territory of the right middle cerebral artery. Three months later he developed epilepsia partialis continua, with clonic jerks of the proximal right upper and lower limbs that were temporally related to PLEDs plus from the right frontal lobe. There was a latency of over 100 milliseconds and a variable relationship of the initial spike of the PLEDs complexes with the clonic movements. Sectioning of the subcortical callosal and projection connections of the frontal lobe abolished the clonic jerks, and later the PLEDs subsided. *Conclusions:* We propose the ipsilateral clonic seizure activity arose from projections from the frontal lobe to the medullary reticular formation as such connections exist and the long and variable latency suggests a polysynaptic system

P-040

Reversible EEG suppression and cranial nerve areflexia in acute hepatic failure

B Young (London), M Sharpe (London)*

Background: Electrocerebral silence in EEG, unless related to drug intoxication or hypothermia is associated with a very poor prognosis for recovery of conscious awareness. We report two cases of acute hepatic encephalopathy associated with severe cerebral edema and loss of cortical EEG activity, who recovered awareness after treatment with hypothermia and mannitol. *Cases:* 2 patients with acute fulminant hepatic failure and cerebral edema became deeply comatose, with loss of most cranial nerve reflexes and marked, generalized EEG suppression. After treatment with mannitol and hypothermia both recovered awareness, showed reduced cerebral edema on CT imaging and regained EEG voltage. *Conclusion:* Acute liver failure with cerebral edema, loss of cranial nerve reflexes and EEG suppression may be reversible. Mannitol and hypothermia appear to be effective treatment strategies.

NEUROMUSCULAR, EMG, NEUROPHYSIOLOGY

P-041

Association of diabetic neuropathy and diabetic retinopathy

Ali Abdollahi (Tehran), Zahra Hallaji (Tehran), Abdolreza Tabasi (Tehran), Baharak Sabet (Tehran)*

Purpose: Diabetes mellitus is a global health problem; retinopathy and neuropathy are two common complications of diabetes. The aim of this study was to evaluate the correlation

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between diabetic retinopathy (DR) and diabetic neuropathy (DN) in type 2 diabetes mellitus. *Patients and method:* In a cross sectional single blind study 100 patients with type 2 diabetes (49 males, 51 females) were studied. Evaluation of peripheral neuropathy was based on clinical symptoms (neuropathic symptom score). Retinopathy was evaluated by indirect ophthalmoscopy. *Results:* Prevalence of neuropathy in patients were 72% and retinopathy was diagnosed in 72% of patients (69.9% NPDR, 30.1% PDR). In total 72 patients had retinopathy, of whom 58 patient had neuropathy (P=0.019) *Conclusion:* Neuropathy coexist with retinopathy in diabetes mellitus type 2 but dose not correlate with type of retinopathy

P-042

Lead neuropathy with histologic similarities to giant axonal neuropathy: A case report

SM Bagshaw (Calgary), JA Pettersen (Calgary), DJ Zuege (Calgary), SM Viner (Calgary), AW Clark (Calgary), B Klassen (Calgary), C White (Calgary)*

Background: Lead toxicity is a rare cause of neuropathy and there are few reports on the electrophysiological and neuropathological correlates. We describe a case of severe predominantly motor axonal neuropathy with histologic similarities to giant axonal neuropathy (GAN). *Methods:* Case report. *Results:* A 66 year-old alcoholic male presented with a 3-week history of fatigue, abdominal pain, anemia, and encephalopathy following heavy consumption of homemade distilled ethanol. Subsequent examination demonstrated flaccid quadriparesis and areflexia. There was no gum lead-line pigmentation. Laboratory studies revealed a normocytic anemia with basophilic stippling, post-transfusion serum lead level of 2.65 µmol/L (normal: 0.0-0.5 µmol/L) and post-transfusion serum 24-hr free erythrocyte porphyrin (FEP) of 5187 nmol/d (normal: 24-190 nmol/d). Electrophysiologic studies were consistent with severe predominantly motor axonal neuropathy. Sural nerve biopsy revealed active axonal and myelin degenerative changes with occasional "giant axons". Focal axonal swellings were seen in tissue sections and along the length of individual axons in teased-fiber preparations. Despite therapy with DMSA (2,3-dimercaptosuccinic acid), an oral chelation agent, the flaccid paralysis persisted with minimal neurologic recovery at five months post-onset. *Conclusion:* This is the first reported case of lead toxicity presenting with severe motor axonal neuropathy and pathologic features similar to GAN.

P-043

CGRP and early rgenerative events

M Bangash (Halifax), D McDonald (Calgary), R Midha (Calgary), D Zochodne (Calgary)*

Abstract Background: Guidance tubes, or conduits that allow direct infusion of molecules into the regenerative microenvironment may allow questions about early regenerative events to be addressed. CGRP (calcitonin gene-related peptide) is a neuropeptide that is prominently expressed in regenerating axons and may influence Schwann cell proliferation, microvascular function and pain generation. Its direct influence on regeneration of nerve, however is not established. *Methods:* In male Sprague-Dawley rats,the left sciatic nerve was transected and the retracted proximal and distal stumps (3 mm apart) were attached to a silastic guidance tube connected to a subcutaneous microinjection port*. The animals were divided into four groups, receiving either CGRP (n=10), anti-CGRP antibody (n=10), hCGRP (8-37), a selective CGRP receptor antagonist (n=10) and carrier Ringer's infusion (n=6) through the injectable port. Regenerative nerve bridges were studied at one week by quantitative immunohistochemistry (using GFAP for Schwann cells; and neurofilament 200 and protein gene product (PGP) 9.5 for axons) and at three weeks for appraisal of myelinated axon regrowth (toluidine blue semithin sections). *Results:* Quantitative immunohistochemical assessment is underway but antagonism of the CGRP receptor or sequestration of its ligand by antibody did not prevent bridge formation or its reinvestment by axons or Schwann cells. Early analysis of myelinated axons suggested differences in myelin thickness among the groups. Further analysis is ongoing and will be presented. *Discussion and Conclusions:* The prominent expression of CGRP in regenerating axons may have important influences on regenerative events and potentially on myelin formation. Its local release, however is not obligatory for early bridge formation. Further analysis of interrupting or enhancing its actions during early and later regenerative events will be important. [Supported by CIHR, AHFMR,CDA]. *D. S. McDonald and D. W. Zochodne, Journal of Neuroscience Methods, Volume 122, Issue 2, 30 January 2003, Pages 171-178

P-044

Reliability of the biceps brachii M-wave

K Calder (Kingston), L-A Hall (St. Catharines), S Lester (Thorold), G Inglis (Grimsby), D Gabriel (St. Catharines)*

Background: The peak-to-peak (P-P) amplitude of the maximum M-wave, and the area of the negative portion of the curve are important measures that serve as methodological controls in H-reflex studies, motor unit number estimation (MUNE) procedures, and normalization factors for voluntary electromyographic (EMG) activity. This study examined the intraclass reliability of these measures for the biceps brachii. *Methods*: Twenty-two healthy adults (4 males and 18 females) participated in 5 separate days of electrical stimulation of the musculocutaneous nerve. A two-factor repeated measures analysis of variance (ANOVA) evaluated the stability of the group means across test sessions. The consistency of scores within individuals was determined by calculating the intraclass correlation coefficient (ICC). *Results:* The P-P amplitude means ranged from 12.67 ± 4.69 mV to 13.21 ± 4.16 mV across test sessions. The group means were highly stable. ICC analysis also revealed that the scores were very consistent (ICC=0.98). The group means for the area of the negative portion of the maximum M-wave were also very stable (33.32 to 35.30 mV‡ms). *Conclusion:* The results support the use of P-P amplitude of the maximum M-wave as a methodological control in H-reflex studies, and as a normalization factor for voluntary EMG.

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P-045

Pilot study on a combined assessment using magnetic resonance spectroscopy and motor unit number estimate in ALS patients

KM Chan (Edmonton), CC Hanstock (Edmonton), C Sorochuk (Edmonton), S Kalra (Edmonton)*

Background: Tools for early diagnosis and disease monitoring in ALS patients are lacking. Magnetic resonance spectroscopy (MRS) and motor unit number estimate (MUNE) are potentially useful biomarkers in quantifying cortical and spinal motoneuronal changes. *Methods:* Three ALS patients along with 3 control subjects each underwent two examinations separated by 4 months. At each session, each subject had a MUNE study using the multiple point stimulation technique on the median-innervated hand muscles and the EDB muscle and a high field 3 T MRS study of the hand and foot regions of the motor cortex. MRS was used to quantify the neuronal and glial markers NAA/Cr and NAA/mI. *Results:* At baseline, the MUNEs in the ALS patients were already markedly diminished and they declined by 12±26% in the hand and by 30±65% in the EDB muscle after 4 months. NAA/Cr was diminished in one ALS patient at baseline. However, there was no consistent change in the spectroscopic indices after 4 months in this small number of subjects. *Conclusions:* MUNE could discriminate ALS patients from healthy controls and was sensitive to disease progression in 4 months. Some abnormalities were also seen in the MRS studies but the pattern was less consistent. These results illustrate the feasibility of combined longitudinal MUNE and MRS assessment in ALS patients. Larger sample size will be needed to determine the utility of this method to aid in early diagnosis and monitoring of disease progression in ALS.

P-046

Congenital axonal neuropathy and encephalopathy associated with central nervous system (CNS) microtubule-associated proteins (MAP) abnormalities and neurofilament swellings.

V Chau (Montréal), J-F Clément (Greenfield Park), G D'Anjou (Montréal), Y Robitaille (Montréal), M Vanasse (Montréal)*

Introduction: Congenital axonal neuropathies (CAN) associated with CNS abnormalities appear to be very rare since only a few cases have been reported in the literature. *Patients:* Over the last twenty years, we have seen eight patients affected by CAN in whom biopsies of sural nerve showed axonal atrophy and loss of large diameter nerve fibres. *Results:* All of these patients presented at birth or soon after birth with hypotonia associated with distal weakness and diffuse areflexia. CNS manifestations included microcephaly, seizures and developmental delay. Outcome was poor as four of them died before age three from respiratory insufficiency or pneumonia. The four surviving patients had severe psychomotor retardation. In the last patient that we have seen, Western blot analysis was performed on snap frozen specimens of temporal and cerebellar cortex and showed absence or hypoexpression of MAP types 1A and 2 as compared to age-matched controls. Callososplenial hypogenesis and neurofilament swellings were also documented in deep white matter and adjacent cortex. *Conclusion:* Congenital axonal neuropathies are rare and most likely represent a group of heterogeneous disorders. Absence or hypoexpression of CNS MAPs has never been reported in congenital neuropathies. This could be a new clinico-pathological entity.

P-047

Association of pseudoxanthoma elasticum with hereditary sensory-motor polyneuropathy: one lesion for two diseases?

D Dowlatshahi (Ottawa), P Chakraborty (Ottawa), P Bourque (Ottawa)*

Background: Pseudoxanthoma elasticum (PXE) is a genetically heterogenous disease where a mutation results in the calcification of elastic fibers in connective tissues. Although neurological manifestations due to disruption of cerebral vasculature are not uncommon in this disease, there has only been one report of peripheral neuropathy associated with PXE. *Methods:* Kinship study. *Results:* We report a 60-year old female with PXE who was noted to have pes cavus, mild weakness in tibialis anterior and hand intrinsic muscles, as well as glove and stocking sensory loss. Nerve conduction studies showed symmetrical conduction slowing in keeping with a demyelinating sensory-motor polyneuropathy. The phenotype was thus consistent with Charcot-Marie-Tooth disease (CMT1). Genetic testing was negative for CMT1A, HNPP and CMTX. The G-banded karyotype was normal. Inquiry into her family history revealed one sister diagnosed with PXE, and one without. Both sisters were subsequently referred for EMG, which revealed asymptomatic polyneuropathies with similar conduction slowing. *Discussion:* One known etiology of PXE is mutation of the ABCC6 gene, located at chromosome 16p13.1. Interestingly, the gene for CMT1C has also been mapped to chromosome 16p13.1-p12.3. We are investigating the possibility that the co-expression of these two rare conditions may be secondary to a chromosome 16p13.1 microdeletion.

P-048

The correlation between the blood ChE activity and brain AChE after organophosphate poisoning

F Fu (Yantai), Y Hou (Binzhou)*

Background: Organophosphates (OPs) are highly toxic compounds that irreversibly inhibit the acetylcholinesterase (AChE)-mediated metabolism of acetylcholine (ACh), which subsequently results in excessive and toxic amounts of extracellular ACh in the cholinergic synapses. Generally the activity of blood cholinesterase (ChE) containing both AChE in red blood cell (RBC) and Butyrylcholinesterase (BChE) in sera was determined to evaluate the effects of AChE reactivator treating the patients with OPs poisoning. The aim of this study is to observe the correlation between the blood ChE activity and brain AChE one. *Methods:* Rabbits were given OPs, including lipid-soluble methyl parathion and water-soluble monocrotophos, and normal saline respectively. The sera, RBC and brain tissues were obtained at different interval after intoxication and the activities of ChE at 1h, 6h and 24h after poisoning were measured by Ellman's method. *Results:* Results showed that AChE activity of brain was paralleled with the one of RBC but not proportional to the BChE of sera no matter how the solubility of OP. *Conclusion:* It suggested that it is the activity of

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RBC AChE but not sera ChE activity which could be used as a marker to represent nervous system levels.

P-049

The change of Acetylcholinesterase level in muscle whose innervating nerve cut

F Fu (Yantai), T Hu (Bonzhou)*

Background: Acetylcholinesterase (AChE, EC 3.1.1.7) is the serine hydrolase responsible for the breakdown of the neurotransmitter, acetylcholine, in the synapse and neuromuscular junction. Two types of enzymes hydrolyze acetylcholine (ACh): AChE, and butyrylcholinesterase (BChE, EC 3.1.1.8) or pseudocholinesterase, which hydrolyze different cholinesters. *Methods:* In order to investigate the change of AChE in muscles the monoclonal antibodies (McAb) were prepared and screened by AChE from brain or RBC and BChE from sera. McAb E6 was recognized a specific one reacting only with brain AChE, nerve AChE. The sciatic nerves of rabbits were cut and the muscles innervated by it were obtained at different intervals. The concentration of AChE was measured by ELISA using McAb E6 as first antibody in order to exclude the contamination of both AChE from RBC and BChE from sera. *Results:* Results showed that the level of AChE in muscle innervated by sciatic nerve was decreased significantly at 0.5h after nerve cut and increased to a level more than that in normal rabbits at 3h but then decreased slightly and near to the normal levels at 12h. *Conclusion:* It suggests that the hydrolase for neurotransmitter would be changed after the nerve was cut and the change of it was time-dependent.

P-050

Analysis of deflazacort treatment of Duchenne muscular dystrophy

R Hung (London), C Campbell (London), S Levin (London), L Bolack (London), C Scholtes (London), B Lyttle (London), C Mitchell (London)*

Background: Deflazacort (DFZ) has been shown to be effective in preserving muscle strength and function, as well as pulmonary function, in Duchenne Muscular Dystrophy (DD), however few randomized trials have been completed making observational studies important. *Study Design:* We retrospectively reviewed all DD patients from a regional pediatric neuromuscular clinic. Twenty eight patients met inclusion criteria with 14 patients treated with DFZ and 14 untreated. Ambulatory status, pulmonary function and side effects were compared. *Results:* DFZ was started at a mean age of 7.47 ± 1.64 years. Initial dose of DFZ was 0.96 ± 0.08 mg/kg/day. Eight of 14 patients treated with DFZ required a wheelchair fulltime (mean age, 10.0 ± 1.5 yrs). Five of the 6 treated patients who were still walking were older than 10 years. Ten of the 14 untreated patients required a wheelchair fulltime (mean age, 10.4 ± 2.2 years). Pulmonary function at age 11 years (percent predicted functional vital capacity) was greater in the treated patients (mean, 92.1 ± 16.1) compared to those untreated (mean, 65.0 ± 19.0) ($p < 0.03$). Scoliosis surgery was required in 3 of 16 untreated patients versus none of those treated. A non-significant increase in mean weight was noted at age 10 years in the DFZ group. There were an equal number of fractures between the two groups. *Conclusions:* DFZ did not delay the time to loss of independent ambulation in our sample, which is in contrast to other studies using similar protocols. DFZ significantly improves pulmonary function in DMD patients. Side effects were not substantially different between the groups.

P-051

Etiology of Oculomotor Palsy: A Case Series of 28 Patients

Ahmad Javadian (Tehran), Abdolreza Tabasi (Tehran), Ali Abdollahi (Tehran), A Dehghani (Tehran), H Mosayebi (Tehran)*

Purpose: To assess the etiology of oculomotor Palsy among 28 patients at Farabi Eye Hospital, Tehran. Iran *Methods:* This case series includes 28 patients with third nerve palsy. The diagnosis were divided into six groups based on symptoms and paraclinical studies: ischemic, traumatic, aneurysm, neoplasm miscellaneous, and undetermined. *Results:* Out of 28 patients, 9(30%) had diabetes mellitus. the chief complaint was mostly ptosis (79%). The pupil was normal in 16 patients (57%) and dialated in 12 patients (43%), The etiology was ischemic in 43%, traumatic in 14%, aneurysm in 7%, tumor in 7%, miscellaneous in 11% and undetermined in 18% of the cases. *Conclusion:* The most common cause of oculomotor nerve palsy is ischemic lesions and the most common risk factor is diabetes mellitus. Further studies to assess the relationship between third nerve palsy and blood sugar control is suggested.

P-052

Isolated neck-extensor myopathy in a patient with Idiopathic Parkinson's Disease

J Kurniawan (Halifax), M Payne (Ottawa), V Bhan (Halifax), R MacAulay (Halifax)*

Background: Isolated neck-extensor myopathy is a rare cause of dropped head syndrome. The pathology usually shows non-inflammatory myopathy. While it can occur in isolation, this entity has been reported in association with parkinsonism, notably Multiple System Atrophy. Here we report a patient with Idiopathic Parkinson s disease (dopa responsive), who later developed a profound head drop, on the basis of isolated neck-extensor myopathy. *Method:* We assessed the patient using standard clinical and laboratory evaluation. We also reviewed the literature. *Results:* Our patient met the criteria for Idiopathic Parkinson's Disease. Five years later she developed subacute onset of a profound head drop. EMG showed changes of an inflammatory myopathy restricted to neck extensors. Muscle biopsy confirmed myopathic changes. CK was normal. Cervical spine abnormalities and anterior neck muscle dystonia were ruled out with appropriate investigations. A trial with oral prednisone showed no significant benefit. Management of the head drop proved very difficult. *Conclusion:* We report a case of isolated neck-extensor myopathy in a patient with Idiopathic Parkinson s Disease. Review of the literature and the significant aspects of our case will be discussed.

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P-053

Parallel lives: Jean-Martin Charcot, Lou Gehrig and amyotrophic lateral sclerosis. An historical vignette

*R Leblanc** (Montreal)*

Introduction: The lives of Jean-Martin Charcot and Lou Gehrig are inexorably linked by the disease that bears their names. *Methods:* Their lives and careers are explored through contemporary texts, letters, photographs, and press reports, and significant parallels are drawn. *Results:* As young men of humble origin and modest means, Charcot and Gehrig benefited from the intervention of a mentor, a thesis supervisor in Charcot's case and a college coach in Gehrig's, to gain entry into their profession. Charcot achieved renown as the discoverer of amyotrophic lateral sclerosis (ALS) and students, such as Babinski and Freud, flocked to his clinic in Paris of the Belle Epoque. His later career was anticlimatic, focusing on hypnosis and faith-healing. Lou Gehrig achieved fame as a star baseball player but as his malady progressed he became the subject of unflattering comments in the press. The dignity with which he confronted his fate and his death at an early age captured the public imagination to an unprecedented degree, and ALS became known as Lou Gehrig's disease. Foundations in his honor continue to support research into ALS to this day. *Conclusions:* Charcot and Gehrig shared many similar life experiences. Each in his way has had a lasting effect on ALS.

P-054

Upper extremity strength in Duchenne muscular dystrophy

S Magalhaes (London), C Campbell (London), L Bolack (London), C Scholtes (London), C Shoesmith (London), S Levin (London)*

Background: Upper extremity (UE) strength and function is known to deteriorate over time in children with Duchenne Muscular Dystrophy (DD), however it is not clear which UE measures are best correlated with general disease progression. This cross-sectional study explores the relationship between disease characteristics and measures of UE strength and function in children with DD. Self rating of performance and satisfaction regarding UE function has not been explored before in DD; the Canadian Occupational Performance Measure (COPM) was used to examine this issue. *Methods:* Fifteen patients with DD, attending a regional pediatric neuromuscular clinic participated in a study of UE strength. Participants rotated through 5 stations including: Brooke UE scale, grip strength and quantitative manual muscle testing (Lafayette system), arm MRC score, timed writing and typing tasks, and the COPM. *Results:* Mean age of participants was 11.17 years. Pearson's correlation analysis of age with outcome measures revealed: a positive correlation with Brooke scale and a negative correlation with left arm MRC score, (-0.528, p less than or equal to 0.05); and was not significant with grip strength and Lafayette system measures. Writing and typing performance improved with age. The Brooke scale and right and left arm MRC scores were highly predictive of one another, (-.0965, -0.955, p less than or equal to 0.001). The COPM showed that subjects were generally satisfied with each identified problem tested (mean equals 73.38%). Performance and satisfaction scores of the COPM were strongly correlated however did not correlate with the other measures. *Conclusion:* MRC scores and the Brooke scale are the best UE measures of stage of disease in this cross-sectional study. Grip strength, writing/typing tasks and the COPM were not found to be indicators of UE stage of disease in this study; this likely reflects the fact that the sample was relatively young.

P-055

Deflazacort stabilizes the spine in non-ambulatory Duchenne muscular dystrophy patients

J Mah (Calgary) , K Lombardo (Calgary)*

Background: Steroids are generally recommended for Duchenne muscular dystrophy (DMD) patients to prolong independent ambulation. However, it is unclear whether these patients should remain on steroids once they become non-walkers. *Methods:* A retrospective review was performed to identify the outcome of DMD patients who received deflazacort for at least three years at the Alberta Children's Hospital between 1991 to 1999. *Results:* Eleven DMD boys received deflazacort (0.9 mg/kg/d) at a mean age of 7.4 (SD 1.9) years, and became wheelchair dependent at 12.8 (SD 2.2) years. Deflazacort was tapered in six (54%) patients after they stopped walking, and their median duration of deflazacort was five (IQR 4-7) years. Five patients remained on deflazacort, with a median duration of eight (IQR 7-12) years. There was no significant difference between the two treatment groups in regards to age, onset of wheelchair dependency, pulmonary function, or cardiac status. Four (67%) patients required spinal fusion within three years after stopping deflazacort, compared to none who remained on deflazacort (p=0.022). *Conclusions:* Deflazacort was beneficial for DMD patients after they lost independent ambulation, by delaying or preventing the progression of scoliosis. Those who came off treatment at this point were more likely to require spinal surgery.

P-056

Sports-related peripheral nerve injuries in children

J Mah (Calgary) , C Adams (Victoria) , C Toth (Calgary)*

Background: Traumatic peripheral nerve injuries are increasingly recognized among children involved in sports. It is helpful to understand the nature of these injuries, in order to identify at-risk individuals and to develop appropriate diagnostic and treatment plans. *Methods:* This was a retrospective review of pediatric electrodiagnostic studies performed at the Alberta Children's Hospital from 2000 to 2004. Children with sports-related neuropathies were identified, and data was collected to identify the mechanism of injuries and their outcome. *Results:* Fourteen (3.7%) out of 377 children had nerve injuries due to sports. Their median age was fourteen years (IQR 11-15), and the majority (78%) were male. Eleven (78%) patients had upper limbs involvement, and five (36%) were associated with bony fractures. Ten (71%) cases were related to motorcross bike racing (3), skate/snowboarding (3), horseback riding (2), or hockey (2). Another four (29%) individuals sustained nerve injuries from playing basketball, rock-climbing, swimming, or weightlifting. Most (77%) mononeuropathies involved the ulnar (4), median (3), or peroneal nerves (3). The majority (86%) improved with conservative management. *Conclusions:* Pediatric sports-related nerve injuries in our series

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were related to compression or traction. Careful clinical and electrodiagnostic assessments were helpful in confirming the location and the extent of injuries.

P-057

A newborn with spinal muscular atrophy type 0 presenting with a clinicopathological picture of centronuclear myopathy.

A Nadeau (Montreal), G D Anjou (Montreal), FG Debray (Montreal), Y Robitaille (Montreal), LR Simard (Montreal), M Vanasse (Montreal)*

Background: Spinal muscular atrophy (SMA) type 0 is a rare lethal neonatal form of SMA due to a deletion or a mutation in the survival motor neuron (SMN) gene. Studying its pathology may help understand SMA pathogenesis and the role of SMN gene in fetal muscle cell maturation. *Methods:* We report a male term newborn in whom the mother noticed reduced fetal movements and who presented at birth with arthrogryposis and severe generalized weakness requiring ventilatory support. There was no family history of neurological diseases. *Results:* Creatine phosphokinase level was mildly elevated (332 U/L). Electromyogram showed polyphasic, small amplitude motor potentials without increased recruitment. Muscle biopsy showed predominant type 1 muscle fibers, muscle fibers atrophy, central nuclei, absence of necrosis, and negative myotubularin immunohistochemical staining, abnormalities suggestive of a severe centronuclear myopathy. Genetic analysis revealed an homozygous deletion of exon 7 on the SMN gene. Mutation analysis of the myotubularin gene on chromosome X is ongoing. *Conclusions:* In this patient with genetically confirmed SMA, muscle biopsy revealed cells resembling myotubes. This may suggest a role of SMN protein in muscle fiber maturation and myotubularin expression and could explain the very early onset of SMA in this patient.

P-058

Bilateral ulnar nerve palsies occuring acutely from repetitive trauma.

C Phan (Edmonton) , Z Siddiqi (Edmonton)*

Background: Ulnar nerve mononeuropathy at the elbow is a very common. We present a rare case of simultaneous and bilateral ulnar nerve palsies after repetitive trauma. *Methods:* Case report *Results:* A 38 year-old healthy right-handed female developed pain, weakness, and numbness of both hands after painting walls with a paint roller and lifting heavy equipment. She had marked weakness and sensory changes in the ulnar nerve distribution bilaterally, but worse on the right. Ulnar motor response demonstrated conduction block in nerve segment around the elbow bilaterally. Inching studies on the right localized the conduction block to a 1-cm segment around the level of ulnar groove. EMG showed denervation pattern in the right first dorsal interosseous and flexor carpi ulnaris. MRI demonstrated a 1.5 cm segment of abnormally increased signal in the right ulnar nerve at the top of the cubital tunnel. Three months after conservative management, repeated NCS showed recovery of CMAP and CV together with clinical improvement. *Conclusions:* The bilateral ulnar neuropathies are secondary to repetitive trauma from sustained and repeated forceful elbow flexion and extension. Brief discussions on elbow mechanics relevant to ulnar nerve injury and the management of ulnar neuropathy will be included.

P-059

Childhood chronic inflammatory demyelinating polyneuropathy (CIDP): evolution, outcome and suggested treatment protocol for refractory cases

E Rossignol (Montréal), M Vanasse (Montréal), G D'Anjou (Montréal), N Lapointe (Montréal)*

Background: Chronic inflammatory demyelinating polyneuropathy (CIDP) represents a group of acquired polyneuropathies evolving over a minimum of two months The pathophysiology of CIDP is not fully understood, but seems to be immune-mediated, through a variety of auto-antibodies and cytokines. Standard treatments recommended are immune-modulators and include IvIG, prednisone and plasmapheresis. The initial response to these treatments is usually satisfactory, but repeated treatments are often needed. In addition, many patients have been considered refractory to conventional therapies and require the use of other immune-suppressant drugs. However, there are no published guidelines to help clinicians in treating those refractory cases. *Methods:* The two last cases of CIDP that we have seen have in our clinic have been refractory to conventional therapies. This prompted us to review the charts of the 12 patients diagnosed with CIDP since 1980 in Hôpital Sainte-Justine. *Results:* Based on this retrospective study, we have evaluated the usual clinical course, treatment response and outcome in our population. *Conclusion:* Based on the review of our cases and of the current literature regarding treatments in adult and pediatric populations, we have elaborated a treatment protocol for refractory cases of childhood CIDP.

P-060

Becker-type dysferlinopathy

M Sinnreich (Montreal), C Therrien (Montreal), G Karpati (Montreal)*

A woman with LGMD2B presented with onset of mild muscular weakness in her fourth decade and remains ambulatory at age 75. Her two daughters were severely affected and wheelchair dependent since their early thirties. Mutational analysis revealed homozygozity for a null allele in both daughters due to a compound mutation [(4872delG) and (4876G>C)]; both parents were heterozygous for this allele. The mother harbored an additional in-frame splice mutation leading to skipping of exon 32, due to an identified A>G substitution of the branch point nucleotide at position 3443-32 in intron 31. In vitro experiments with recombinant mini-genes confirmed the implication of the intronic branch point nucleotide mutation in skipping of exon 32. While Western blot showed absence of any dysferlin immunoreactivity in skeletal muscle of both daughters, the mother harbored reduced levels of a shortened dysferlin protein, possibly retaining sufficient biological activity to account for her significantly milder phenotype. The compound heterozygozity of the mother expressing a shortened dysferlin protein and having a milder clinical phenotype is reminiscent of the constellation seen in patients with "Becker-type" dystrophinopathies who express truncated forms of dystrophin and have a milder disease

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than "Duchenne" patients. A "Becker-type" dysferlinopathy has not been reported to date.

P-061

Local dystrophin expression in nine Duchenne muscular dystrophy patients after intramuscular normal-myoblasts injections.

D Skuk (Québec), M Goulet (Québec), B Roy (Québec), JP Bouchard (Québec), P Chapdelaine (Québec), JG Lachance (Québec), M Sylvain (Québec), JP Tremblay (Québec)*

In non-human primate experiments, two conditions are important for the success of myoblast transplantation (MT): myoblast delivery by a protocol of high-density intramuscular injections and appropriate immunosuppression. Presently, we are testing these conditions for MT in Duchenne muscular dystrophy (DMD). Nine DMD patients received myoblasts obtained from skeletal-muscle biopsies of normal donors. These cells were injected in 1 cm^3 or less of the Tibialis anterior by 25 or 100 parallel injections. Similar patterns of saline injections were performed in the contralateral muscles. The patients received tacrolimus for immunosuppression. Muscle biopsies were performed at the injected sites 4 weeks later. We observed donor-dystrophin-positive myofibers or a significant increase of dystrophin-positive myofibers only in the cell-grafted sites of 8 patients. The percentage of donor-dystrophin positive myofibers, for the total number of myofibers in the biopsies, varied from 3 to 26 percent donor-dystrophin transcripts or a significant increase of dystrophin transcripts were detected by RT-PCR only in the cell-grafted sites of the 9 patients. In conclusion, significant dystrophin expression can be obtained in the skeletal muscles of DMD patients following specific conditions of cell delivery (high-density intramuscular injections) and an appropriate control of acute rejection.

P-062

First test of a high-density intramuscular injection protocol for normal-myoblast transplantation throughout several skeletal muscles in a Duchenne muscular dystrophy patient.

D Skuk (Québec), M Goulet (Québec), B Roy (Québec), V Piette (Québec), C Côté (Québec), JP Bouchard (Québec), JG Lachance (Québec), M Sylvain (Québec), JP Tremblay (Québec)*

We tested for the first time the safety and the effects of a high-density injection protocol for myoblast transplantation (MT) throughout entire skeletal muscles in a Duchenne muscular dystrophy (DMD) patient. The patient (26 years old, severely affected by the disease) received myoblasts cultured from a normal donor, delivered by injections as close as 1-mm apart throughout skeletal muscles in one arm (biceps brachium, brachoradialis, thenar and hypothenar groups) and in 2 cm^3 of gastrocnemius. Tacrolimus was used for immunosuppression. Histological studies done in biopsies performed at the injected sites in the gastrocnemius 1 month after MT, showed 40-50 percent dystrophin-positive myofibers in the cell-grafted site, and none in the contralateral, saline-injected site. Functional evaluations done in the arm up to 6 months later after MT showed some improvements in the force and amplitude of flexion in the 1st metacarpian and the amplitude of flexion-extension in the elbow. The only consequences of the procedure were local reactions that generally resolved in a week. Thus, MT by high-density injections throughout several muscles was well tolerated, and allows observing many dystrophin-positive myofibers in muscles with severe atrophy and fat infiltration. Functional improvements were observed, in spite of the absence of placebo as control.

Movement Disorders

P-063

Mild vascular risk factors are not associated with worsened parkinonsism in older patients with Parkinson's disease.

A Currie (Halifax), R Camicioli (Edmonton), W Martin (Edmonton), T Roberts (Edmonton)*

Abstract: *Background:* The presence of vascular risk factors (VRF) may affect the severity of motor signs in patients with Parkinson's disease (PD). *Objectives:* To determine whether older PD patients with VRF have more severe parkinsonsim than those without. *Methods:* Electronic records from the Movement Disorders Clinic at the University of Alberta identified patients with PD. VRFs were identified in patients with idiopathic PD, 65 years of age and older. Part III of Unified Parkinson's Disease Rating Scale (UPDRS), and the Mini-Mental Status Scale (MMSE), were recorded. Patients were divided into the following groups: 1) PD without VRF; 2) PD with VRF; 3) PD-Dementia (PDD) without VRF; and 4) PDD with VRF. Demographics, UPDRS, and MMSE were compared. *Results:* A total of 382 PD patients were identified. Groups did not differ in age. There was no difference in UPDRS scores between PD without VRF (n=143, mean+/-sd, 22+/-13) and those with VRF (n=191, 23+/-12) or between PDD patients without (n=25, 32+/-13) or with VRF (n=23, 32+/-14). UPDRS scores were higher ($p<0.0001$) in PDD compared to PD. MMSE did not differ between PDD groups. *Conclusion:* Vascular risk factors did not influence overall motor impairment in older PD patients regardless of the presence of dementia.

P-064

Sequencing of the candidate gene LAMA1 in DYT15 locus for myoclonus-dystonia

F Han (Ottawa), L Racacho (Ottawa), D Bulman (Ottawa), D Grimes (Ottawa)*

Background: Mutations in the epsilon-sarcoglycan (SGCE) gene at 7q21 have been shown to cause myoclonus dystonia (MD) in approximately 50% of cases. A new locus (DYT15) at 18p11 was identified in a Canadian family (family A). Given that patients with mutations in SGCE are indistinguishable from patients linked to DYT15, we proposed that the DYT15 protein is playing a role similar to that of SGCE. LAMA2 is part of the dystroglycan complex as is SGCE. Within the DYT15 locus we identified the gene LAMA1. Similar structural roles between LAMA1 and LAMA2 makes LAMA1 a strong candidate for DYT15. *Methods:* 62 exons and 2 kb of the promoter region of LAMA1 were sequenced in 8 SGCE negative MD families. *Results:* 30

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polymorphisms, 12 of them novel were found but no disease-causing mutations were identified. Interestingly, between exon 22 and exon 44 of LAMA1, there is a 38 kb homozygous region shared by affected individuals from families A and B, implicating these two families are related. *Conclusions:* In addition to six STS linked markers, this 38 kb shared homozygous region of LAMA1 suggests that a common mutation exists that causes myoclonus-dystonia in these two families. Taken together, this would narrow the DYT15 locus to a 2.13 Mb region. Despite LAMA1 being an attractive candidate no mutations were found by direct sequencing.

P-065

Emergency department usage among movement disorder patients.

J Larsen (Saskatoon), M Rajput (Saskatoon), A Rajput (Saskatoon)*

Background: The purpose of the study was to characterize patterns of emergency department (ED) use by patients with movement disorders (MD). *Methods:* This was a retrospective study using a convenience sample of Movement Disorder clinic patients. A questionnaire asked general demographic data and details of any ED visits from June 1, 2003 to May 31, 2004. Further details including discharge diagnosis were abstracted from patient records. *Results:* Analysis shows that ED visits were not associated with gender, type of movement disorder, location of home (urban vs. rural), distance to the ER, level of education, or employment status (full-time, part-time, unemployed, on disability or retired). Those who live in long-term care were the least likely to utilize ED services. Of 92 MD patients, there were 22 visits to the ED (26%). Of the patients with Parkinson's disease (PD), 30% visited the ER in the past year. Of those patients with non-PD MD, 19% had ED visits. *Conclusions:* Through understanding the patterns of emergency department use by patients with MD, we could provide earlier intervention, improved management of complications of chronic disorders, and ultimately reduce the need for ED services within this population.

P-066

In vitro characterization of bioreactor-expanded human neural progenitor cells for cell restoration strategies

K Mukhida (Halifax), M McLeod (Halifax), M Hong (Halifax), D Sadi (Halifax), A Sen (Calgary), M Kallos (Calgary), B Baghbaderani (Calgary), L Behie (Calgary), I Mendez (Halifax)*

Background: Stem cells show properties of self-renewal and multipotentiality and are attractive candidates for cell restoration strategies. Protocols to rapidly expand human stem cells for extended periods of time without losing these characteristics have been established using bioreactors. A project was undertaken to characterize the immunohistochemical phenotypes of human neural progenitor cells (HNPCs) derived from different regions of the fetal brain and expanded in bioreactors. *Methods:* HNPCs were isolated from the telencephalon, ventral mesencephalon, brain stem, and spinal cord of eight to ten week gestational aged human fetuses. HNPCs from the telencephalon and brain stem were expanded in bioreactors. Bioreactor- and non-bioreactor- expanded HNPCs were differentiated in vitro for seven days and examined immunohistochemically for neuronal, astroglial, oligodendroglial, and stem cell phenotypes. *Results:* Independent of the region of tissue origin, both bioreactor- and non-bioreactor-expanded HNPCs demonstrated immunoreactivity for beta-III tubulin, indicative of differentiation into immature neurons. Furthermore, bioreactor-expanded cells also demonstrated immunoreactivity for both tyrosine hydroxylase and glutamic acid decarboxylase. *Discussion:* Fetal-derived HNPCs can be isolated, expanded in bioreactors, and differentiated into neurons in vitro. Optimal yield of neuronal differentiation may be reliant on additive instructive signals in culture or the gestational age at tissue procurement.

NEUR-ONCOLOGY

P-067

Anti-Ma - associated encephalitis mimicking Progressive Supranuclear Palsy

A Bay (Ottawa), P Bourque (Ottawa)*

Background: Ma proteins represent a family of onconeural antigens that are expressed in neurons, germ cells of the testis and in several types of tumors, with a marked predominance of testicular neoplasms. Anti-Ma antibody-associated paraneoplastic syndromes are increasingly recognized and appear to differ from classical limbic encephalitis. *Case report:* We report the case of a 34 year old man who was successfully treated by orchiectomy for a limited stage seminoma. Six months prior to the discovery of the testicular neoplasm, he had presented with a progressive unexplained neurologic syndrome similar to PSP: parkinsonism, bilateral hyperreflexia, complete vertical and horizontal saccadic paralysis (with preserved oculocephalic eye movements), lack of response to dopaminergic therapy. Enhanced MRI of the brain was normal. CSF was normal except for the presence of oligoclonal bands. Both serum and CSF were positive for Ma1 and Ma2 antibodies. There was little response to steroids and IvIg, but a moderate improvement in gait and mobility was noted following monthly cyclophosphamide therapy. Oculomotor deficits have not improved and he requires additional treatment for complex partial seizures. *Conclusions:* The presence of CSF oligoclonal bands and the intrathecal expression of anti-Ma antibodies clearly suggest an autoimmune pathophysiology and paraneoplastic etiology. This case illustrates the predominance of limbic, diencephalic and brainstem involvement in anti-Ma associated neurologic syndromes.

P-068

Papillary glioneural tumor: a case study with five decades of follow-up

C Berk (Halifax), RAS Reid (Halifax), DB Clarke (Halifax), R Macaulay (Halifax)*

Background: Papillary glioneuronal tumor (PGNT) is a rare variant of mixed neuronal-glial neoplasms. Most of the previously described cases have occurred in adolescents and young adults. Due to short follow-up periods, there is limited knowledge of the natural history of this lesion and its prognosis, such that the best

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management strategy remains uncertain. *Methods:* This case report describes a left temporal PGNT in a 66-year-old man who presented with medically refractory epilepsy. *Results:* Neuro-imaging studies over the 11 years prior to his recent surgery demonstrated little tumor growth and stable contrast enhancement. This patient had subtotal resection of a lesion in the same location 52 years earlier. *Conclusions:* Our case provides the longest reported follow-up of a patient diagnosed with PNGT. Pathological examination of this enigmatic tumor supports the classification of PGNT with ganglioliomа rather than with dysembryoplastic neuroepithelial tumors (DNET). This patient's several-decade clinical history is consistent with PGNT's biological behavior as a very benign and indolent tumor.

P-069

Alteration of response to cell death stimulation in glioblastoma cells deficient in DNA-dependent protein kinase

GG Chen (Hong Kong), FLF Sin (Hong Kong), BCS Leung (Hong Kong), WS Poon (Hong Kong)*

Cells lacking or with dysfunctional DNA-dependent protein kinase (DNA-PK) are often associated with mis-repair, chromosome aberrations and complex exchanges, all of which contribute to the development of human cancers including glioblastoma. Two human glioblastoma cell lines were used in the experiment, M059J cells lacking the catalytic subunit of DNA-PK, and their isogenic but DNA-PK proficient counterpart, M059K. We found that M059K cells were much more sensitive to staurosporine (STS) treatment than M059J cells, as demonstrated by MTT assay, TUNEL detection and annexin V- and propidium iodide staining. A possible mechanism responsible for the sensitivity in these two cell lines was indicated by the expression of Bcl-2, Bax, Bak and Fas. The cell death stimuli increased anti-apoptotic Bcl-2 and decreased pro-apoptotic Bcl-2 members (Bak and Bax) and death receptor (Fas) in glioblastoma cells deficient in DNA-PK. Activation of DNA-PK is known to promote cell death of human tumor cells via modulation of p53 activities. Apoptotic signaling by p53 may down-regulate the anti-apoptotic Bcl-2 member proteins and induce pro-apoptotic Bcl-2 family members. Taken together, our findings suggest that DNA-PK has a positive role in the regulation of apoptosis in human glioblastomas. The aberrant expression of Bcl-2 family members and Fas was, at least in part, responsible for decreased sensitivity of DNA-PK deficient glioblastoma cells to cell death stimuli.

P-070

In vitro study of anti-glioma activity of autologous cytokine-induced killer cells

*Z-p Chen * (Guangzhou), L Lin (Tiamjing)*

Background: Cytokine-induced killer (CIK) cells have been found to possess higher anti-tumor activity due to the high proliferation of double CD3+ and CD56+ positive cells. This study was designed to investigate the anti-glioma activity of CIK cells in vitro. *Methods:* The CIK cells were generated by incubation of peripheral blood monocytes (PBMCs) of the patient with glioma in the presence of various types of cytokines. The CIK cells were stained with PE anti-human CD3 antibody and cychrome anti-human CD56 antibody to determine the immunophenotype with FACScaliber flow cytometer. The cytotoxic effect of CIK cells against glioma cells (glioma cell line SF-295) was determined by MTT reduction assay. *Results:* (1) The CIK cells showed dual staining of CD3+CD56+ with positive rate of 3.45% on day 10 and 55.2% on day 30 of incubation. (2) Antitumor activity of CIK cells in vitro showed that, with the ratio of effector and target cells at 25:1, 50:1 and 100:1, the killing rate was 37.12%, 60.69% and 71.08%, respectively. At ratio of 50:1, the killing rate on the day of 10, 18, and 26 was 52.39%, 67.31% and 58.89%, respectively. *Conclusion:* The CIK cells derived from the patient with glioma were predominantly CD3+CD56+ dual positive cells with the highest antitumor activity in vitro up to 2-3 weeks.

P-071

How well do housestaff diagnose brain tumor in patients using clinical data alone?

C DeSilva (London), R Hammond (London), J Megyesi (London)*

Background: In many medical institutions around the world patients harboring an intracranial mass lesion undergo initial assessment by medical or surgical housestaff. Using a combination of patient demographics, history, physical examination and their own clinical experience a provisional diagnosis is formed which is used to guide further investigations. This study assesses the accuracy of these provisional diagnoses for a variety of intracranial mass lesions. *Methods:* Two hundred cases of patients with an intracranial mass lesion that had a pathological diagnosis determined at the London Health Sciences Center between 1999 and 2004 were identified. Final pathological diagnoses for these lesions were then classified into seven categories: high grade glioma (HGG), low grade glioma (LGG), metastases, meningioma, lymphoproliferative disorder (LPD), abscess and reactive tissue. The initial assessments performed on these patients prior to any imaging were reviewed and summarized into one-paragraph synopses by the study team. These included any relevant facts from the history of presenting illness, past medical history and physical examination as well as both patient age and sex. These 200 cases were then presented separately to four neurosurgical housestaff at different levels of training to make a total of 800 readings. Their provisional diagnoses were then compared with the final pathology. *Results:* The 200 cases identified included 103 males and 97 females with a mean age of 58.2 years. Overall the housestaff correctly diagnosed the lesion in 452 out of 800 cases (57%). Accuracy varied substantially between the diagnostic categories: HGG (62%), LGG (36%), meningioma (45%), LPD (27%), metastases (78%), reactive tissue (29%) and abscess (25%). Accuracy was 57% for housestaff at the beginning of their training and 56% for those at the end. *Conclusions:* In this study, neurosurgical housestaff were correct 57% of the time when making a diagnosis based on clinical data alone. The number of years of training did not appear to affect accuracy. The results suggest that more malignant lesions such as HGG and metastases are more readily diagnosed than more indolent lesions such as LGG and meningioma when using clinical data alone.

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P-072

Neuroimaging and neuropathology in pediatric posterior fossa tumors

C DeSilva (London), A Ranger (London), R Hammond (London), J Megyesi (London)*

Background: The goals of this study were 1) to determine how well the neuroimaging diagnosis correlates with the final pathological diagnosis, and 2) to determine how well the frozen section diagnosis correlates with the final pathological diagnosis in pediatric patients with posterior fossa brain tumors. *Methods:* The charts of 25 pediatric patients who underwent surgery for posterior fossa brain tumors at the London Health Sciences Centre were reviewed. The neuroimaging reports (MRI and/or CT), the frozen section pathology reports and the final pathology reports for each patient were independently analyzed and compared. The final pathology report was deemed to represent the correct diagnosis. *Results:* In the pediatric population studied there were 14 males and 11 females with an overall mean age of 7.9 years. MRI was used in 24/25 patients (96%). Neuroimaging correlated with final pathology in 10/25 patients (40%). In 8/25 patients the neuroimaging diagnosis did not correlate with final pathology, while in 7/25 patients the neuroimaging diagnosis was indeterminate. Sensitivity of neuroimaging was 50% for ependymoma, 38% for medulloblastoma and 45% for low grade glioma. Positive predictive value was 50% for ependymoma, 38% for medulloblastoma and 83% for low grade glioma. Frozen section data was available for 21 patients. The frozen section diagnosis correlated with the final pathological diagnosis in 20/21 patients (95%). Sensitivity was 100% for ependymoma, 100% for medulloblastoma and 89% for low grade glioma. Positive predictive value was 100% for all tumor types. *Conclusion:* At present neuroimaging alone cannot be used to reliably diagnose posterior fossa tumors in the pediatric population. However, frozen section pathology correlates very well with final pathology in these tumors.

P-073

Radiosurgery induced meningioma in a neurofibromatosis type 2 patient

S Di Maio (Vancouver), R Akagami (Vancouver)*

Background: We report the case of a young patient with neurofibromatosis type 2 (NF-2) whose acoustic neuromas had been treated with gamma knife radiosurgery, one of which was associated with the development of a 6 cm "kissing" acoustic neuroma and atypical meningioma recurrence. *Methods:* The English language literature was reviewed regarding complications of radiosurgery in NF-2 patients. Our patient with a major recurrence of the acoustic neuroma and an adjacent atypical meningioma 5 years after radiosurgery is reviewed retrospectively. *Results:* Although it is generally felt that radiosurgery may not be as effective in control of NF-2 related acoustic neuromas compared with sporadic tumours, radiosurgery is more commonly being used to help manage these difficult tumours. NF-2 patients are often not included in reports on secondary neoplasms due to their underlying tumorigenic tendencies, and few reports are available on possible secondary tumors in NF-2 after radiosurgery. *Conclusion:* The challenges in managing the recurring tumours in this 19-year-old female are presented. Continued surveillance and reporting of patients are required.

P-074

Intraneural hemangioma of the brachial plexus

J Golan (Montreal), D Tampieri (Montreal), MC Guiot (Montreal), L Jacques (Montreal)*

Introduction: Intraneural hemangiomas of peripheral nerves are benign and very rare lesions. Angiography has rarely been used in their management. *Methods:* We recently encountered and treated a patient with this unusual lesion at the Montreal Neurological Hospital. A systematic review of the English and French literature was performed. *Results:* The patient was a 40 year old woman who presented with a right-sided neck mass, radiating pain down the ulnar side of the arm when coughing, and a positive Tinel's sign on exam. Magnetic resonance imaging demonstrated a lesion compatible with a nerve sheath neoplasm. Initial surgical exploration revealed a very bloody tumor that resembled a hemangioma on frozen section. Angiography and embolization of feeding vessels were necessary before a second surgical exploration was undertaken. The lesion was involving the inferior trunk and could only be partially resected. Pathological examination confirmed an intraneural hemangioma. Thirty four hemangiomas of peripheral nerves have been described and only two of these have involved the brachial plexus. This is the only reported case in which embolization was a useful adjunct to surgery. *Conclusion:* Intraneural hemangiomas are rare benign lesions. Angiography and embolization may be required to achieve adequate resection.

P-075

Gamma knife surgery in the management of vestibular schwannomas

C Kazina (Winnipeg), A Kaufmann (Winnipeg), M West (Winnipeg), G Schroeder (Winnipeg), J Nesbit (Winnipeg), H Long (Winnipeg)*

Background: In Canada, there has been a relatively low utilization rate of radiosurgery such as Gamma Knife Surgery (GKS) due to limited availability and recognition. The introduction of a high volume GKS unit in Winnipeg is anticipated to have a significant impact on Vestibular Schwannoma (VS) management. *Methods:* All VS cases treated at the Winnipeg Centre for GKS in its first year of operation were reviewed. GKS utilization rates and referral patterns for these tumors were analyzed. In addition, tumor characteristics, previous management strategies and early follow-up data were reviewed. *Results:* 45 patients (22 from Manitoba) with VS were treated at the Winnipeg Centre for GKS in its first year. Indications for treatment included radiographic tumor growth, symptom progression, and functional preservation. 30 of these patients had received no previous treatment while 15 had previous surgical resection. 83% of the patients who were previously untreated had functional hearing. *Conclusions:* GKS is becoming increasingly recognized as a standard treatment option (primary or adjuvant) for VSs. As such, a major shift is being observed from the traditional treatment options to GKS where appropriate. The greater than anticipated number of VS cases from Manitoba reflect a

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backlog of tumors to be treated as well as expanding indications for GKS.

P-076

Idiopathic hypothalamic dysfunction associated with neural crest tumours: Case report and review of a new pediatric paraneoplastic syndrome.

A Kirton (Calgary), B Trussell (Calgary), D Stother (Calgary), K Barlow (Calgary), E Wirrell (Calgary)*

Background: Idiopathic hypothalamic dysfunction (IHD) is a rare disease of children that has recently been associated with neural crest malignancies. Clinical features include obesity, adipsic hypernatremia, impaired thermal regulation, personality change, multiple hypothalamic-pituitary-axis abnormalities and nondescript weakness. *Methods:* Case Report. *Results:* A 5 year-old girl presented with progressive proximal weakness, inability to walk and leg pains over 3 days. She received the influenza vaccination two days prior to symptom onset. Thoracic ganglioneuroblastoma was treated successfully 2.5 years earlier. Relevant examination findings included proximal grade 2-3 power and absent ankle-jerk reflexes. She was diagnosed with probable Guillain-Barre syndrome (GBS) and started on IVIG. Serum sodium was subsequently measured at 182 mmol/L with euvolemia and impaired thirst. Excessive weight gain, gynecomastia, heat intolerance, and personality change over the past year were subsequently appreciated. CSF demonstrated a lymphocytic pleocytosis (WBC 20) with normal protein while ESR (22), CK (580), and prolactin (65) were mildly elevated. Strength normalized within 48 hours. MRI of the brain/hypothalamus and nerve conduction studies were normal while metanephrine and MIBG studies did not suggest tumour recurrence. Temperature remained 38-39ºC without evidence of infection. *Conclusion:* IHD is associated with neural crest malignancies and can present with weakness mimicking GBS.

P-077

Lhermitte-Duclos disease and Cowden disease: clinical and genetic characterization of a case

G Lapointe (Quebec), P Lavoie (Quebec), R Laframboise (Quebec), P Gould (Quebec), A Turmel (Quebec)*

Objective: To review the clinical presentation of a patient with a case of Lhermitte-Duclos associated with Cowden disease and to review the current literature. *Method:* A 28 year old man with a history of migraine, splenomegaly and multiple lipomas was brought to our attention after experiencing severe headaches, nausea, vomiting and diplopia for more than two weeks. The initial physical examination demonstrated bilateral horizontal nystagmus, papilloedema, skin lesions, macrocrania, gingival hypertrophy, poor dental hygiene and thyroid nodules. The patient did not present any specific neurological sign. The initial CT Scan and MRI demonstrated a large cerebellar lesion located in the right hemisphere compatible with Lhermitte-Duclos disease, cerebellar tonsils herniation and obstructive hydrocephalus. *Results:* A posterior fossa craniectomy, partial resection of the cerebellar mass confirming gangliocytoma and C1 laminectomy were performed and the patient's symptoms improved. Futhermore, the patient underwent a complete investigation for Cowden disease, including neuropsycological evaluation, medical photographs and genetic testing which came back positive for PTEN mutation. *Conclusion:* Cowden disease and Lhermitte-Duclos disease have been associated as being a possible new phakomatosis. Genetic testing, family screening and extensive investigation are part of the adequate treatment of the patients presenting with this association.

P-078

Intraventricular seeding of a central neurocytoma

*R Leblanc** (Montreal) , M-C Guiot (Montreal)*

Background: Central neurocytomas (CN) are recently recognized intraventricular tumors whose natural history is not fully understood. We describe the case of a patient with a CN of the right lateral ventricle that seeded to the left temporal lobe 30 years after the initial diagnosis. *Case report:* A 19 year-old woman had a CT scan which demonstrated a highly calcified, cystic, thalamic lesion extending into the right lateral ventricle. She remained asymptomatic for 20 years when the cystic component enlarged to produce hemiparesis. Stereotactic cyst aspiration and biopsy revealed a benign CN. She later developed hydrocephalus which responded well to shunting, following which she was treated with radiotherapy. She remained stable until the age of 48 years when an MRI scan demonstrated a new lesion involving the left temporal lobe originating from the subependymal layer. Histopathological examination identified a benign CN. *Discussion:* CNs have been recognized as a distinct entity since 1982. They classically involve the lateral, third and fourth ventricles in that order, and only rarely are intraparenchymal. Our case indicates that CNs can have a very indolent course. These tumors should be followed with regular examinations and neuro-imaging since they can enlarge locally and they can seed through the ventricular system.

P-079

Endoscopic-assisted transsphenoidal endonasal approach to sellar lesions

*B Lo** (Hamilton), K Reddy (Hamiton)*

Introduction: Endoscopic-assisted transsphenoidal endonasal surgery has advantages of minimal invasion and excellent visualization. Image guidance is used to compensate for lack of stereoscopic vision. A washing device is used to keep the endoscopic view clear. *Methods:* 34 sellar lesions were resected using this approach from April 1, 2002 to August 31, 2004 at the Hamilton Health Sciences Centre. *Results:* 17 males, 17 females. Median age: 51 (30 - 84). 29 cases of pituitary adenoma (average 1.8 cm). Other cases: Rathke's cyst, fungal hyphal mass, lymphoma, en plaque meningioma, CSF leak due to middle cranial fossa defect. Presenting symptoms: visual defect-7, headaches-13, acromegaly-1, Cushing's disease-5, diabetes insipidus-4, apoplexy-2, aseptic meningitis-1, CSF leak-1, Addisonian crisis-1, galactorrhea-amenorrhea-infertility-3. 30-degree endoscope was used in 4 cases, 45-degree endoscope in 9 cases. Operative time for pituitary adenomas: 100 minutes. Image guidance used in all cases. Nasal difficulties: 1 case of curved septum, 1 case of mucocele of sphenoid sinus. Abdominal fat graft in 25 of 34 cases. Recurrence of pituitary lesions in 2 cases. 1 case of post-operative hemorrhage with

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apoplexy. 1 case of post-operative CSF leak. Blood loss averaged < 200 cc. 9 patients received radiation. *Conclusion:* Endoscopic-assisted approach to sellar lesions is effective with minimal invasion and excellent visualization.

P-080

Heavily calcified pituitary macroadenomas: a case report & review of literature

*B Lo** (Hamilton), K Reddy (Hamilton)*

Introduction: Calcifications are infrequently observed in pituitary adenomas. Both radiologic and pathologic studies quote frequencies of less than 10%. Calcospherites can transform the pituitary tumour into a pituitary stone. Mechanism of calcospherite formation has been elucidated. *Case Report:* A 61 year-old man with underlying bladder cancer and chronic renal insufficiency presented to the Hamilton General Hospital with a 3.7 cm pituitary macroadenoma. Both CT and MRI revealed a heavily calcified mass that extends suprasellarly in a cauliflower-like manner. Endoscopic-assisted endonasal transsphenoidal resection of the lesion was performed. The lesion has a pearly white gross appearance. Pathological examination shows immunopositivity for prolactin and extensive areas of calcifications. No complications were noted post-operatively. Patient continued to be treated with bromocryptine. Post-operative residual tumour is noted with consideration for craniotomy for gross total resection. *Conclusions:* The exact mechanism of pituitary calcospherite formation has not been elucidated. However, prolactin granules have been characterized as sulfated glycosaminoglycans and glycoproteins. This is probable source of calcifiable matrix. Excessive intracellular concentrations of calcium have also been shown to promote cell degeneration and necrosis. Cellular debris is identified around the self-propagating calcified dense bodies.

P-081

Radiosensitizing Rat Glioma Using L-Buthionine SR-Sulfoximine (BSO)

KA Mannan (Saskatoon), BH Juurlink (Saskatoon), RW Griebel (Saskatoon)*

Background: The treatment of GBM remains a great challenge with no significant advances during the last two decades. The prognosis for patients with GBM remains poor despite multimodality treatment including surgery, radiotherapy, and chemotherapy with a mean survival of approximately one year. Elevated levels of glutathione are found in many tumors including brain tumors and are thought to play a role in tumor resistance to chemo and radiotherapy. Treatment with Buthionine-L-(SR)-sulfoximine (BSO) causes tissues or cells with moderate to high rates of glutathione turnover to be depleted of glutathione. *Methods:* A rat glioma model was produced by stereotactically injecting C-6 glioma cells into the right brain hemisphere. The presence of the tumors was confirmed using MRI 12 days post implantation. Using convection enhanced delivery we injected BSO into the tumors of the experimental group. *Results:* The glutathione content of the tumors was reduced by more than 70% of their baseline value. Subsequent treatment with radiotherapy resulted in survival rates that were much higher than the control group. *Conclusions:* Reducing the glutathione content of glioblastoma in a rat model using BSO greatly increased their survival rates following radiotherapy. With further studies and evaluations, this may be a promising avenue for improving survival rates in patients with GBM.

P-082

CNS lymphoma/lymphomatoid granulomatosis with inconclusive antemortem pathological diagnosis

J Marriott (Ottawa), M Sharma (Ottawa), J Woulfe (Ottawa)*

Background: Lymphomatoid granulomatosis (LG) is an uncommon disorder affecting the central nervous system. The association between LG and lymphoma is uncertain and a definitive antemortem diagnosis is often difficult. *Methods:* A 57 year old female was admitted to our institution with a history of progressive weakness and cognitive dysfunction over three months. During a six-month period the patient underwent numerous investigations including lumbar punctures, multiple cranial MRIs and biopsies of the liver, lung, brain and bone marrow. An autopsy was performed. *Results:* The extensive investigations detailed above were inconclusive. The patient was first treated empirically for CNS vasculitis and after clinical and radiological progression with chemotherapy for Non-Hodgkins lymphoma. Finally interferon was initiated after a tentative diagnosis of LG. The patient continued to deteriorate and died six months after presentation. At autopsy, the bulk of the cerebral pathology was suggestive of LG, however isolated areas of B-cell lymphoma were also observed. *Conclusion:* This case highlights the diagnostic and therapeutic challenges in LG and LG-related lymphoma. Irrespective of prognosis, the delay in diagnosis is harmful to patients and families. The diagnostic process is discussed. Strategies to increase diagnostic accuracy, including multiple stereotactic biopsies, are presented.

P-083

Acute clinical deterioration of a cerebellopontine angle schwannoma due to brain stem dysfunction

Nancy McLaughlin (Montreal), France Berthelet (Montreal), Michel W Bojanowski (Montreal)*

Background: Schwannomas represent slowly growing tumors. Usually, symptoms install progressively. Rarely, intratumoral hemorrhage or hydrocephalus occur and are responsible for rapid onset symptomatology. We present a unique case of sudden deterioration resulting from brain stem dysfunction. *Methods:* Case report and literature review. *Results:* 30-yr-old male was admitted comatose with decerebration after sudden loss of consciousness. He had complained of intense headaches and hearing impairment since several weeks. Cerebral tomography revealed a hypodense mass at the right cerebellopontine angle with a cystic component, heterogeneous enhancement, and mass effect on the brain stem. No acute intratumoral or intracystic hemorrhage or hydrocephalus were documented. The tumor was approached by a retromastoid sub-occipital craniotomy. Histopathological examination confirmed the diagnostic of schwannoma and revealed an unusual significant lymphoplasmocytic infiltration. The patient evolved remarkably. No acute deterioration has recurred since surgery. *Conclusion:* This is a unique case of a tumor of the cerebellopontine angle manifesting

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itself by a sudden loss of consciousness in the absence of intratumoral or cystic hemorrhage or hydrocephalus. Although the precise eotiology of the brain stem dysfunction remains to be elucidated, the important inflammatory process highly unusual for schwannomas might contribute to this unique clinical presentation.

P-084

Radioresistance of human glioblastomas : Modulation by green tea polyphenol (-) epigallocatechin-3-gallate

N McLaughlin (Montreal), B Annabi (Montreal), J-P Bahary (Montreal), R Moumdjian (Montreal), R Beliveau (Montreal)*

Background: The combination of radiotherapy and chemotherapy has been envisioned as a therapeutic approach for glioblastoma multiforme (GBM). GBM's aggressiveness is however potentiated in those radioresistant tumor cells that had escaped apoptosis. The goal of this study is to elucidate if epigallocatechin-3-gallate (EGCg), a green tea-derived anti-cancerous molecule, can increase GBM's response to ionizing radiation (IR). *Methods:* Human GBM-derived U-87 cells were cultured and transfected with cDNA coding for Survivin, an inhibitor of apoptosis protein, then treated with EGCg. Mock and transfected cells were irradiated at sublethal single doses. Proliferation was assessed by nuclear cell counting and protein expression by western blotting. *Results:* IR (10 Gy) reduced mock U-87 cell proliferation by 40% through a caspase-3 independant mechanism. The overexpression of Survivin induced a cytoprotective effect against IR. Pretreatment of the cells with EGCg overcame the prosurvival effect of recombinant Survivin and decreased cell proliferation. This suggests a potential therapeutic effect of EGCg in synergy with IR and targeting prosurvival intracellular pathways. *Conclusion:* GBMs' radioresistance is possibly mediated by a mechanism dependent of Survivin. The combination of natural anti-cancerous molecules such as EGCg with radiotherapy could optimize the efficacy of current IR treatments.

P-085

Ependymoma of the pituitary fossa: case report and review of the literature

K Mukhida (Toronto), S Asa (Toronto), F Gentili (Toronto), P Shannon (Toronto)*

Background: Ependymomas are glial neoplasms that comprise 1.2 to 9% of all primary intracranial brain tumours. Although some arise in the parenchyma without an obvious association with the ventricular system, reports of ependymomas in the pituitary fossa have been documented only three times in humans. The case of a pituitary fossa ependymoma, including its immunohistochemical and ultrastructural characteristics, is described. *Methods:* A 43 year old man with no significant past medical history presented with a one-year history of decreased libido. His systemic and neurological examinations were normal. Laboratory investigations revealed panhypopituitarism. Magnetic resonance imaging demonstrated a well-demarcated enhancing lesion that displaced the optic chiasm. The lesion was completely resected transphenoidally. *Results:* The patient's post-operative course was uneventful. Histology revealed characteristic though subtle perivascular nuclear free zones composed of spindled glial elements with numerous well-formed ependymal rosettes. Electron microscopy confirmed the presence of typical intercellular junctions and large bundles of intermediate filament. *Conclusions:* The pituitary fossa is a rarely documented site of ependymomas. This is the first study that examines the electron microscopic appearance of a pituitary ependymoma. The theories of the origin and treatment of these rare tumours are discussed in the context of the literature concerning other intracranial ependymomas.

P-086

Granular cell tumor of a spinal nerve root, a case report and review of the literature

L Ogieglo (Saskatoon), M Kelly (Saskatoon), C Beavis (Saskatoon), L Allen (Saskatoon), R Griebel (Saskatoon), L Resch (Saskatoon)*

Background: Granular cell tumors are a rare form of neoplasm and are thought to arise from Schwann cells of peripheral nerves. We report the second known case of a granular cell tumor arising from a spinal nerve root. *Methods:* A 13 year old female presented with a right S1 radiculopathy and normal motor, bowel and bladder function. Magnetic resonance imaging revealed an intradural, extramedullary lesion arising off of the right S1 nerve root. The tumor was intimately associated with both the ventral motor and the dorsal sensory rami of the S1 nerve root on operation. En bloc excision was not possible without sacrifice of the nerve root. In order to preserve function, intralesional/marginal resection was performed. Histopathological analysis revealed a granular cell tumor. *Conclusions:* Granular cell tumors arising from spinal nerve roots are exceedingly rare. We report the second known case of this entity and describe our management.

P-087

Inhibition of TGF-b1 expression in malignant glioma cell lines by using antisens oligonucleotide incorporated in custom-made liposomes

Marie-Eve Potvin (Sherbrooke), Robert Adams (Sherbrooke), David Fortin (Sherbrooke)*

Neoplastic transformation involves the accumulation of genetic alterations which allow cells to bypass restriction points from normal cell cycle. Some growth factors are overexpressed and contribute to development of neoplasic phenotype by stimulating cell proliferation, invasion, angiogenesis and escape from the immune system. TGF-b1 (transforming growth factor beta) is one such factor. This protein stimulates tumor growth, cell migration, and plays a role in resistance to cellular death in malignant gliomas. We have already presented data supporting the overexpression of the active counterpart of this protein in different malignant glioma cell lines (F98,-118, G-373). Oligonucleotide antisens molecules against mRNA typically inhibit transcription of the protein coded by binding specifically to the mRNA, blocking transcription of the final product. By the use of a high affinity antisens oligonucleotide against TGF-b1, incorporated in a custom-made cationic liposome optimized to penetrate the target nepolastic cells, we undertook the suppression of TGF-b1 in these cell lines. This suppression

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produced a decrease in tumor growth as asseyed with WST-1 proliferation assay, and a decrease in individual cell motility, as evaluated by a morphometric analysis of tridemensional grown F98 spheroids.

P-088

Bleomycin treatment of cystic craniopharyngiomas (CP)

D Simonyan (Quebec), L Cantin (Quebec), C Picard (Quebec), Y Samson (Quebec), L Blondeau (Quebec), A Turmel (Quebec)*

Introduction: The treatment of CP of children is a therapeutic challenge. Although direct surgery is considered the gold standard, the complications are frequent, especially in retro-chiasmatic types. Delaying of radiotherapy in young children is also desirable. Bleomycin has been shown to have an effect in cystic CP. *Methods/Results:* A 6 year old girl presented with visual symptoms. In spite of two supra-tentorial and one trans-sphenoidal surgeries she had recurrence of the CP. Radiotherapy was instituted but development of a cyst necessitated the placement of an Ommaya reservoir. Bleomycin was administrated according to the Vancouver protocol. The cyst disappeared without recurrence. A 12 year old boy presented with increased ICP due to a retro-chiasmatic CP. An Ommaya reservoir was placed stereotactically and Bleomycin was administrated accordingly. A partial response was observed (< 50 % decrease in cyst volume). He developed visual symptoms. Mechanical aspiration further diminished the cyst but he was still symptomatic. MRI revealed progression of the solid component. A trans-sphenoidal decompression was performed. *Conclusion:* Cystic craniopharyngiomas are sensitive to Bleomycin, but the response rate is uncertain. Patients should be carefully monitored by endocrinology, ophthalmology and serial MRIs. Bleomycin can be part of the treatment of cystic craniopharyngiomas but does not exclude surgery or radiotherapy.

P-089

Childhood meningioangiomatosis (MA): case report and review of literature

D Simonyan (Quebec), P Gould (Quebec), C Picard (Quebec), A Turmel (Quebec), L Cantin (Quebec)*

Background: MA is a rare, benign tumor. Since its first description in 1915 medical literature has furnished fewer than 100 cases of this lesion. MA exhibits a wide spectrum of clinical, imaging and histological features, making diagnosis difficult. We present one case of MA with long-term follow-up and review of literature. *Methods:* We described a case of MA at the CHA - Hôpital de l'Enfant-Jésus, Quebec. Clinical features, results of imaging and EEG were obtained. The histopathological, immunohistochemical and ultramicroscopic exams were performed for pathological diagnosis. Pathogenesis was discussed. Data of surgical outcome were analyzed through clinicians' interviews and control MRIs during seven years after surgery. Literature review was conducted by searching all articles available on the subject in Blackwell Synergy, Ovid Technologies, PubMed, SciELO, UpToDate. *Results:* Our case confirms the common trends of MA described in the medical literature: a)60% of patients are children and young adults b)Male > Female c)Sporadic MA > MA associated with NF-2,NF-1 d)CT scan: hypo-density of the lesion with calcification; MRI: hypo- or iso-intensity in T1-weighted and hyper-intensity in T2-weighted images. e)Pathologically MA present a vascular and meningothelial proliferation of leptomeninges and adjacent cortex with numerous calcifications. f)Surgical treatment with total removal of the lesion gives seizure-free outcome in 43-68% of MA without recurrence of tumor in most of cases. *Conclusions:* 1.MA is a rare benign tumor with uncertain pathogenesis. 2.The pre-operative diagnosis is difficult because clinical and imaging features are non-specific. 3.There are rather typical pathological characteristics of MA. 4.A total removal of the lesion has good prognostic with absence of recurrence of tumor and seizures.

P-090

Paraneoplastic limbic encephalitis case report: post-neoplastic or a new association with glioblastoma multiforme?

M Sproule (London), P O'Connor (Toronto)*

Background: Paraneoplastic limbic encephalitis (PLE) is a rare disorder most commonly associated with small cell lung carcinoma. *Case Report:* We present the case of a 55-year-old woman with a history of breast cancer (1991) and endometrial cancer (1992) who presented with a three-month history of short-term memory loss in January 2004. Antineuronal antibody tests were positive for N-type calcium channel autoantibodies. An MRI of the brain revealed abnormalities within the medial temporal lobes involving the hippocampal and parahippocampal areas. Extensive imaging investigations and a breast biopsy were unremarkable for the presence/recurrence of an underlying malignancy. In July 2004 the patient developed seizures with further short-term memory deterioration. Following a seizure in November, she was brought to the ICU where an MRI showed a large bilobulated mass lesion suggestive of a high-grade glioma. She continued to deteriorate and died shortly after. A bitemporal glioblastoma multiforme was identified on autopsy. No other source of malignancy was found. *Conclusion:* This is the first reported case of PLE involving antineuronal antibodies detected years after the treatment of the inciting tumor(s). This suggests that the syndrome may be the end result of long-term immunologic damage following cancer treatment. Alternatively, PLE in this case may have heralded her glioblastoma multiforme, the first reported association of PLE with this neoplasm.

P-091

Malignant spindle cell tumor of the brain post radiotherapy - case report

A Szymczak (London), S Krawitz (London), L Ang (London), D Macdonald (London), J Megyesi (London)*

Background: There have been many case reports outlining how radiation to the central nervous system can induce neoplasms such as meningiomas and sarcomas. Here we present the unusual case of patient with a meningioma that transformed into a malignant spindle cell tumor post radiotherapy. *Clinical Presentation:* A 77-year-old right-handed female initially presented to another institution in 1992 complaining of balance problems and a right foot drop. Neuroimaging revealed a left parietal brain lesion consistent with a meningioma. She subsequently underwent surgical resection and the

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pathology revealed a fibrous meningioma. Due to recurrences of the meningioma she underwent multiple surgeries between 1995 and 2001 being left with a dense right-sided hemiparesis. In 2003 she received 24 treatments of radiation to the recurrent meningioma. Six weeks after radiotherapy a mass was noted to be protruding through the skull superior to the site of the meningioma. The mass enlarged to approximately 10 x 5 centimeters, located atop the skull. It was weeping and hemorrhagic in nature. Referral was made to our institution. *Intervention:* Preoperative embolization resulted in a good reduction of blood supply to the tumor. Surgical resection of the extracranial portion of the tumor was performed. This required resection of a large amount of bone that appeared to be involved with infiltrating tumor. Only a small amount of tumor was identified within the intracranial compartment. A near total resection was performed. The cranial defect was repaired with an acrylic cranioplasty. The plastic surgery service performed a skin graft. The patient was clinically unchanged postoperatively. Pathological analysis revealed a high grade sarcoma with myofibroblastic features. Microscopic tumor was identified in the bone. *Conclusion:* We present a case of a 77-year-old female with a known fibrous meningioma, which has transformed into a malignant spindle cell tumor post radiotherapy. Only a few such cases have been described in the literature. This is the only one with such a prominent extracranial component to the tumor.

P-092

Development of symptomatic postural hypotension after resection of fourth ventricular tumors: case reports

S Vachhrajani (Toronto)*

Background: Postural hypotension involves neurological and non-neurological etiologies, and causes major medical and psychological morbidity. Numerous management strategies exist for this condition. Disruption of the sympathetic limb of the baroreflex arc makes it a presenting feature of posterior fossa tumors. There are no reported cases of orthostatic hypotension occurring after tumor resection. *Methods:* Two patients underwent resection of 4th ventricular primary tumors complicated by post-operative postural hypotension. Charts were reviewed, and literature searched for similar cases. Neurophysiology of the baroreceptor reflex arc was reviewed. Several management options were attempted, and a new strategy involving erythropoieitin was also employed after failure of established therapies. *Results:* No other similar cases of orthostatic hypotension were found. We postulate that this complication is secondary to baroreflex pathway disruption at the ventrolateral medulla and the nucleus tractus solitarius. This complication is refractory to conservative management, and outcomes were equivocal after erythropoeitin treatment. *Conclusions:* Two new cases of orthostatic hypotension after recent resection of 4th ventricular tumors are presented. Neuronal damage to the nucleus tractus solitarius and ventrolateral medulla near the floor of the 4th ventricle is responsible. Established therapies are not efficacious; new strategies are not convincing. Further study will be needed to further define the neurophysiology and develop more effective treatments.

P-093

Cerebellar hemangioblastomas in children

M Vassilyadi (Ottawa), E Ventureyra (Ottawa), J Michaud (Ottawa)*

Background: Cerebellar hemangioblastomas in children are rare benign neoplasms of blood vessels of unknown histogenesis. *Methods:* The database of all children with brain tumors operated on at the Children's Hospital of Eastern Ontario in the last 30 years was reviewed. *Results:* Two patients were identified to have hemangioblastomas out of 306. Both were females aged 18 months and 15 years at the time of diagnosis. They presented with signs and symptoms of increased intracranial pressure and a cystic cerebellar hemisphere lesion with mass effect and obstructive hydrocephalus, suspected to be a pilocytic astrocytoma. Both underwent craniotomy and successful total excision of the tumor with no complications or tumor recurrence. For the first case, the histological diagnosis was made on the permanent pathology sections, whereas for the second case the vascular lesion was suspected to be a hemangioblastoma intraoperatively. Neither patient had Von Hippel-Lindau's disease. *Conclusions:* Review of the world literature has revealed few case reports of cerebellar hemangioblastomas in children, with two or less cases in large series. Complete surgical excision of these lesions is the treatment of choice. Nevertheless, the size, location and tumor vascularity can influence both the resectability of these lesions as well as the operative outcome.

Degenerative Disorders, Demenita

P-094

Subjective memory complaints in Chinese subjects with Mild Cognitive Impairment

Helen Fung Kum Chiu (Hong Kong SAR), Linda Chui wa Lam (Hong Kong SAR)*

Subjective Memory Complaints in Chinese subjects with Mild Cognitive Impairment. *Background:* Prospective studies of Mild Cognitive Impairment (MCI) suggested that this condition represents a possible prodrome of dementia with a high likelihood of further cognitive and functional deterioration. As the diagnostic criteria for MCI still awaits further refinement, the presence of subjective memory complaints remains central to the discussion. *Method:* The present study aims to evaluate the significance of subjective memory complaints in a group of ambulatory Chinese elderly subjects with MCI. Participants, aged over 65, were evaluated using a brief memory questionnaire, Clinical dementia rating (CDR), Chinese versions of mini-mental state examination (CMMSE), category verbal fluency test (CVFT), digit and visual span tests, Alzheimer's disease assessment scale - Cognitive subscale (ADAS-Cog). *Results:* 235 subjects were assessed; 94 were cognitively intact normal controls (NC) with CDR of 0; 66 were MCI subjects with only memory and orientation problems (MCI not demented, MCIND)(CDR, 0.5); 75 subjects were MCI subjects with memory problems and subtle functioning changes (MCI possible incipient dementia, MCIID)(CDR, 0.5). The NC group had significantly fewer memory complaints than other groups (Kruskal

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Wallis test, chi square = 11.2, df 2, p< .005). The number of memory complaints was significantly associated with ADAS-Cog total (Spearman rho = .2, p< .005) and subscale scores of immediate recall (Spearman rho = .2, p< .005). Logistic regression revealed that memory complaint was a significant predictor for MCIID, but not MCIND. *Conclusion:* The use of a brief memory inventory was helpful for the screening of memory problems in Chinese subjects with MCI, particularly for subjects with subtle functional deterioration.

P-095

The Alzheimer's disease gamma-secretase partitions into lipid rafts in the lysosome.

M Kirchhof (London), J Madreanas (London), S Pasternak (London)*

Background: Beta-amyloid is produced by the sequential proteolytic cleavage of the amyloid precursor protein (APP), first by a beta-secretase and then by a gamma-secretase (a complex of proteins including presenilin, Nicastrin, mAph-1 and Pen2). Many lines of evidence have suggested that cholesterol and by extension, cholesterol lowering drugs can modulate the production of beta-amyloid. One possible mechanism for this is that the interactions of APP with its processing enzymes may be regulated by sequestration in detergent resistant membrane regions termed lipid rafts. *Methods:* Using the tritosome technique, we have produced highly purified lysosomes from the rat liver. Lipid rafts were isolated by density gradient centrifugation. Cholesterol was selectively depleted using methyl-beta-cyclodrextrin. Enzyme assays were performed using commercially available fluorogenic substrates (Chalbiochem). *Results:* We have previously demonstrated that gamma-secretase proteins and activity are highly enriched in the lysosome. Here we show that these proteins partition within lysosomal lipid rafts. As such, their association and biochemical activity is sensitive to detergent and cholesterol concentrations. *Conclusions:* This work demonstrates that gamma secretase proteins in the rat liver are enriched in lipid rafts. Our results suggests that the lysosomal lipid raft compartment contributes to the generation of beta-amyloid.

P-096

Influence of Encephalomalacia on EEG and MRI findings in Creutzfeldt-Jakob Disease

J Marriott (Ottawa), M Sharma (Ottawa), G Jansen (Ottawa)*

Background: Sporadic Creutzfeldt-Jakob (CJD) is the prototypic human prion disease. Although most patients develop clinical and paraclinical evidence of diffuse cerebral dysfunction, isolated cases of focal symptoms and/or focal pathology have been reported. The association between focal EEG and MRI abnormalities co-localizing to an area of previous traumatic brain injury has not been reported. *Methods:* A 56 year old female was admitted to our institution with rapidly progressive cognitive deterioration resulting in death. Serial EEG and MRIs were performed as part of our investigations. *Results:* The patient's clinical course and postmortem pathology was consistent with sporadic CJD. Serial EEG and MRI scans demonstrated focal abnormalities co-localizing with an area of encephalomalacia secondary to a remote motorcycle accident. As the patient's clinical status worsened, these abnormalities became more diffuse. A definitive diagnosis of CJD was made at autopsy. *Conclusions:* The association between focal abnormalities in CJD corresponding to a previous traumatic brain injury has not been described previously. Our case is compared and contrasted with published reports of focal abnormalities in CJD. The potential reasons for the lateralizing findings in our patient are discussed.

P-097

Calcium-imbalance: the single disease of the man?

A Palotas (Szeged, Hungary), G Laskay (Szeged, Hungary), B Penke (Szeged, Hungary), L Kemeny (Szeged, Hungary), Z Janka (Szeged, Hungary), J Kalman (Szeged, Hungary)*

Introduction: Efforts to elucidate the pathomechanism of beta-amyloid peptide and its precursor protein in Alzheimer's disease and other factors in diverse neurodegenerative disorders have yielded an increasing pile of hypotheses. When analyzing thousands of scientific papers, the involvement of the central secondary messenger, calcium, becomes apparent. *Methods:* Resting intracellular calcium concentration of neurons, glias, fibroblasts and lymphocytes were assessed utilizing comparative fluorimetric methods with or without treatment of cultures with beta-amyloid. Amyloid-precursor-protein levels and gene-expression profiles were determined using Western-immunoblot and DNA micro-chips. Medline search was performed to supplement and justify the involvement of calcium in various neurodegenerative disorders. *Results:* Disturbed calcium homeostasis is present in all cell-types examined after beta-amyloid treatment. Medline-search points out the role of calcium disregulation in several neurometabolic disorders, including schizophrenia, Parkinson's, Huntington's, amyotropic lateral sclerosis, etc. Metabolites of the amyloid-precursor are strongly associated with calcium-induced cellular changes both at the proteomics and genetics level as confirmed by immunoblot and gene-chip analysis. *Discussion:* Our results and data from Medline-search confirm that calcium imbalance might be a common underlying factor in brain pathologies. Disturbed calcium interferes with some of the many biochemical pathways characteristic of a certain disorder, determined by environmental and genetic factors, yielding disease-specific pathologies. Both calcium-mediated neuroprotection and neurotoxicity, therefore, is proposed in this study. By targeting calcium, this new information promises to broaden our understanding of health and illness and the approaches we take to treating disease.

Multiple Sclerosis / Inflammatory

P-098

Apoptosis-related genes as markers of disease subtypes and treatment response in multiple sclerosis

A Hebb (Halifax), V Bhan (Halifax), J Fisk (Halifax), J Murray (Halifax), L Stefura (Halifax), R Soundararajan (Halifax), C Moore (Halifax), H Robertson (Halifax), J Gillard (Montreal), G Robertson (Halifax)*

Background: The clinical course of MS includes relapsing-remitting (RR), secondary-progressive, primary-progressive and

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benign. Early identification and treatment of more aggressive forms of MS may slow disease progression. A failure of autoreactive T cells to undergo apoptosis may contribute to the pathogenesis of MS. The role of the inhibitors of apoptosis (IAP) family of anti-apoptotic proteins such as XIAP, HIAP-1 and HIAP-2 in RR, secondary-progressive, primary-progressive or benign forms of MS is unclear. *Methods:* Peripheral blood mononuclear (PBMN) and T cells were isolated from blood of 40 MS patients and 12 control subjects. Gene expression and protein levels were assessed by quantitative real-time polymerase chain reaction (qRT-PCR) and western blotting, respectively. *Results:* RNA analyses performed on 40 MS patients and 12 normal control subjects suggest a trend for XIAP and HIAP-2 induction in PBMN and T cells, respectively, from patients with a more severe MS disease course. Protein analyses showed an increase in XIAP from PBMN cells from MS patients with a more severe disease course, including RR and secondary progressive types of MS, relative to normal control subjects. *Conclusions:* The present findings suggest that specific patterns of blood lymphocyte IAP expression are associated with a more active MS disease course.

P-099

Rasmussen's encephalitis and bilateral facial myoclonus in a 58 year-old woman

G Hunter (Saskatoon), J Donat (Saskatoon), W Pryse-Phillips (St. Johns), S Harder (Saskatoon), C Robinson (Saskatoon)*

Background: Rasmussen's encephalitis is generally considered to be a disease of childhood, the vast majority of cases occurring in children less than 10 years of age. We report the case of a 58 year-old previously healthy female with clinical, radiological, and histopathological evidence of Rasmussen's encephalitis, representing the oldest known case to date. *Methods:* Case Report *Results:* A previously healthy 58-year-old woman presented with complex partial seizures characterized by staring spells and left facial numbness. A subtle hypodensity of the right temporal-parietal region was seen on CT, and corresponded with an area of T2 hyperintensity on MRI. Two weeks later the patient had developed dysarthria and twitching of the left facial muscles. She later developed synchronous involvement of the tongue, palate, and right facial muscles, and cognition deteriorated. Repeat MRI revealed extension of the lesion. Biopsy showed inflammatory changes consistent with Rasmussen's encephalitis. The patient initially had some response to IVIG, but continues to suffer from spastic weakness of the left hand with ongoing facial myoclonus. *Conclusions:* Rasmussen's encephalitis is generally a disease of childhood but should be considered in the differential diagnosis for adults with chronic progressive focal encephalitis and epilepsia partialis continua. IVIG should be employed as first line therapy for adults with Rasmussen's encephalitis.

P-100

Optimum experimental conditions for the measurement of myo-inositol at 3 tesla using magnetic resonance spectroscopy.

S Kalra (Edmonton), C Hanstock (Edmonton)*

Background: Proton magnetic resonance spectroscopy (MRS) allows for the measurement of the neuronal and glial markers N-acetylaspartate (NAA) and myo-inositol (mI). Whereas NAA quantification is simple and reliable, quantification of mI is technically challenging. Our objectives were to determine the optimum experimental conditions for combined NAA and mI detection on a 3 tesla MR system and to evaluate the reproducibility of the spectral intensity ratios. *Methods:* Optimum sequence timings were determined using a computational spectrum simulation method. Phantom and human MRS experiments using a STEAM sequence followed to determine the minimal voxel size that produced adequate signal over noise. Seven healthy subjects underwent two MRS exams of the motor cortex separated by 4 months. *Results:* The optimum sequence timings were a mixing time of 40 ms and an echo time of 160 ms. The minimum voxel size was 2 x 2 x 3 cm. The coefficients of variation (100%*standard deviation/mean) were: NAA/Cr=9.9%, mI/Cr=19.5%, and NAA/mI=23.5%. *Conclusions:* Optimum experimental conditions are provided for the measurement of NAA and mI using high field MRS. These results are applicable to the study of degenerative disorders where neuronal degeneration and astrogliosis coexist.

P-101

3T high field single voxel magnetic resonance spectroscopy of multiple sclerosis patients with and without gadolinium enhancing white matter lesions

C Nunweiler (Vancouver), A Traboulsee (Vancouver), E MacMillan (Vancouver), A Mackay (Vancouver), D Li (Vancouver)*

The goal of this study was to determine if the white matter N-acetylaspartate/ creatine (NAA/Cr) ratio of normal appearing white matter for multiple sclerosis (MS) patients with Gadolinium enhancing lesions differed from that for patients without gadolinium enhancing lesions. Fifteen patients with clinically definite MS with at least one clinical relapse in the past year, and not currently on disease modifying therapy were recruited for possible entry into a clinical treatment trial. A brain MRI and magnetic resonance spectroscopy (MRS) was performed on all patients using a single box-like voxel centered over the corpus callosum. Spectra were analyzed by a single evaluator blinded to the presence or absence of gadolinium enhancing lesions. The NAA/Cr and choline/creatine (Cho/Cr) ratios for those MS patients who had, or did not have, gadolinium enhancing lesions were compared using a students t-test for significance at a p value of <0.05. Four of the patients had at least one enhancing lesion. Comparison of both ratios did not demonstrate a significant difference in the mean ratios between the two groups. This result suggests the NAA content of a large sample of predominantly white matter centered over the corpus callosum may be independent of current focal lesion activity.

P-102

Psychotic disorders in multiple sclerosis.

SB Patten (Calgary), LM Metz (Calgary), LW Svenson (Edmonton)*

Background: Psychotic disorders are believed to occur with increased frequency in people with multiple sclerosis (MS). However, the literature contains only case-reports and case-series. Our goal was to determine whether psychotic disorders are

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associated with MS in the general population. *Methods:* The analysis was based on administrative data from an Alberta Health Care Insurance Plan. Analysis included data from 2.45 million Albertans who were at least 15 years of age in 2002. Subjects receiving two or more physician diagnoses of MS or of psychotic disorders between 1994 and 2003 were identified. Tabular analyses and logistic regression were used in the analysis. *Results:* The dataset included 10,368 subjects with MS, a prevalence of 0.42%. The prevalence of organic psychosis was 0.50% and of non-organic psychoses was 1.3%. Logistic regression adjusting for age and sex determined that both non-organic and organic psychoses were significantly associated with MS. The strength of the association depended on age, but not on sex. The highest prevalence of both organic and non-organic psychosis was in the 65 and over age group. The strongest association was found in the 15-24 age group where the OR for organic psychoses was 11.1 ($p < 0.0001$) and for non-organic psychosis was 6.6 ($p < 0.0001$). *Conclusions:* The prevalence of psychotic disorders is substantially elevated in people with MS. Additional research is required to determine the clinical significance, etiology and treatment needs of this population.

P-103

Variant Alzheimer disease with spastic paraparesis: Phenotype-genotype correlation of a presenilin-1 exon 8 P264L mutation

JA Pettersen (Calgary), B Curry (Calgary), PH St. George-Hyslop (Toronto), DG Patry (Calgary)*

Introduction: Variant Alzheimer disease (varAD) with spastic paraparesis is an autosomal dominant early-onset dementia characterized by beta-amyloid positive "cotton wool" plaques and an underlying mutation of the presenilin 1 (PS-1) gene, most commonly an exon 9 deletion. *Methods:* Case Report. *Results:* A 57 year-old female died following a 15-year history of arm myoclonus, 5-year history of progressive cognitive decline, and 2-year history of gait problems and upper motor neuron signs in the legs. Family history was positive for dementia and gait problems affecting the patient s mother, maternal uncle and 2 maternal aunts. Multiple investigations, including genetic testing for Huntington's disease, did not reveal an etiology. Neuropathology at autopsy was notable for diffuse large eosinophilic beta-amyloid positive "cotton wool" plaques, along with congophilic angiopathy, neuritic plaques and neurofibrillary tangles. Spinal cord sections revealed loss of myelin in the corticospinal tracts. On genetic sequencing, a point mutation in PS-1 exon 8 (P264L) was evident, consistent with a diagnosis of varAD. C*onclusions:* VarAD with spastic paraparesis is a rare neurodegenerative disorder caused by a PS-1 gene mutation. To our knowledge, there has only been one family reported in the literature with this specific phenotype caused by exon 8 P264L mutation.

P-104

Evidence for retinal autoimmunity in multiple sclerosis

M Sproule (Toronto), F Forooghian (Toronto), C Westall (Toronto), L Gordon (Los Angeles), G Jirawuthiworavong (Los Angeles), K Shimazaki (Los Angeles), P O'Connor (Toronto)*

Background: Multiple sclerosis (MS) has been associated with uveitis, suggesting an immunological link between the uvea and CNS in MS. The retina is embryologically derived from the CNS, and it is conceivable that retinal antigens may be recognized by the immune system in MS. This study was performed to further explore and elucidate the presence of retinal autoimmunity in MS. *Methods:* Thirty-four patients with clinically definite MS and thirty-eight controls were recruited. All patients and controls had a standard electroretinogram (ERG) performed in addition to a special brightflash protocol to isolate photoreceptor function. Patient and control sera were analyzed for antiretinal antibodies using Western blot techniques. *Results:* We found statistically significant differences between patients and controls in three ERG parameters. In the MS group, implicit times of the mixed response b-wave and brightflash a-wave were reduced, as were the amplitudes of the photopic oscillatory potentials. Patients with the highest antiretinal antibody titres had reduced ERG responses. *Conclusions:* We report electroretinographic evidence of retinal dysfunction, including the first evidence of photoreceptor dysfunction, in MS. These ERG findings were associated with antiretinal antibody titres in some of the patients. The discovery of autoimmunity in the unmyelinated retina suggests that non-myelin antigens may play an important role in the pathogenesis of MS.

P-105

Informal support and loneliness among persons with multiple sclerosis (MS) residing in continuing care centres (CCCs)

S Warren (Edmonton), K G Warren (Edmonton)*

Background: About 10% of MS patients reside in CCCs, but few studies have described these residents' experiences. Some healthcare professionals have expressed concern that family/friends do not provide enough informal support to MS patients in CCCs. Methods: Data collected by Alberta Health and Wellness using a minimum data set tool was analyzed to examine informal support to persons living in CCCs across Alberta. *Results:* 96 of the randomly sampled 1845 CCC residents had MS. The mean hours of informal support per week (standard deviation) received by MS patients was 47.2 (18.1) compared to 53.6 (24.3) by other residents (p less than .05). For MS patients, weekday mean hours were 3(6) and weekend 3(8); for other residents, weekday mean hours were 4(12) and weekend 2(5). More MS patients (43.8%) were left alone for long periods of time than other residents (34.1%) (p less than .05). Despite their differences, no more MS patients (25.0%) than other residents (27.3%) indicated feeling lonely. *Conclusion:* There may be a ceiling level of informal support necessary to avoid loneliness so that, while MS patients received fewer hours of support from family/friends and were left alone longer, the majority still had enough support to prevent loneliness.

P-106

Suicide in multiple sclerosis patients exposed to disease modifying therapy

R Zabad (Calgary), D Lavorato (Calgary), S Patten (Calgary), L Svenson (Calgary), M De Jesus (Calgary), L Metz (Calgary)*

Background: The Calgary Treatment Outcomes Study describes long-term safety and outcome data in a population-based cohort of active relapsing-remitting MS patients exposed to disease modifying therapy. We describe mortality due to suicide over the first 5 1/2

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years of follow-up. *Methods:* Baseline and annual demographic and clinical data have been collected in this dynamic cohort study since January 1, 1999. Reported deaths are recorded and confirmed and patients that fail to attend for annual follow-up are tracked. Date and cause of death are verified through medical chart review, from a previously identified contact person or physician, and from provincial registry data. Provincial age and sex specific suicide and overall mortality rates for all Albertans and for those with MS are used to calculate standardized mortality ratios (SMR). *Results:* The ever-treated population includes 1213 patients and 4401.56 person-years of data. There were 14 deaths including 6 suicides. The SMR of death due to any causes in this treated cohort was 1.16 (95%CI: 0.63, 1.95) using 2001 Alberta population data. The SMR for death due to suicide was 6.92 (95% CI: 2.54, 15.05). *Conclusions:* This study demonstrates a high rate of suicide compared to the Alberta population. Ongoing analysis will determine if suicide is more common in this treated MS cohort than in the Alberta MS population. The association between suicide and MS treatment is unclear. It may relate to having MS or to psychological factors if treatment did not match expectations.

Spinal Disorders

P-107

The GLAST and GLT1 glial glutamate transporters are potential neuroprotective targets in spinal cord injury

M Alhejji (Calgary), FW Yang (Calgary), S Casha (Calgary)*

Introduction: Following neural-trauma glutamate transporters may promote glial uptake and limit extra-cellular glutamate concentrations and thus excitotoxicity. Alternatively, reversed glutamate transport may exacerbate changes in extra-cellular glutamate and promote excitotoxicity. *Methods:* In a rat clip compression model of spinal cord injury (SCI), expression of the glial glutamate transporters GLAST and GLT-1 was evaluated using western blotting and immunohistochemistry. Intraperitoneal TBOA (a pan inhibitor of these transporters) was administered prior to injury and the effects on cell markers (NF200 and GFAP) was evaluated by western blotting. *Results:* Following SCI both GLAST and GLT1 expression increased at 6, 12 and 24 hours. Higher expression of both proteins was seen in the dorsal horn grey matter with diffuse expressed in the remaining grey matter. No significant expression was seen in white matter. Double labeling immunohistochemistry revealed expression of both transporters in both neurons and astrocytes after injury. Degradation of NF200 seen after SCI was ameliorated at 6 and 24 hours with TBOA. GFAP expression was unchanged. *Discussion:* Changes in protein expression of glial glutamate transporters suggest that they may have a role in the pathophysiology of SCI. Inhibition of these transporters may be neuroprotective as evidenced by decreased axonal protein breakdown after SCI.

P-108

A national survey of one-level lumbar discectomy: preliminary results.

A Cenic (Hamilton), E Kachur (Hamilton)*

Background: To ascertain Neurosurgical practices in the management of one-level lumbar discectomy in the Canadian adult population. *Methods:* One page questionnaire faxed to each Neurosurgeon in Canada with questions relating to their practice in the management of this common neurosurgical procedure. All data analyzed using Microsoft Excel. *Results:* After the first round of faxes, 89 completed surveys were returned giving a 56% response rate with the respondents being predominantly adult neurosurgeons (86%). Of the respondents, 90% perform lumbar discectomy. Only 17% of respondents had a spine fellowship. For preoperative imaging, 40% use BOTH CT and MRI whereas 28% use only MRI and 19% use only CT. Prior to initial skin incision, 60% use a localization X-ray image. Preoperative antibiotics are prescribed by 93% of respondents. Majority of respondents (63%) use a pre-incision local anesthetic, whereas no agreement for pre-closure intramuscular injection was obtained. With respect to magnification, 74% use microscope, 19% loupes, and 4% none. Only 14% use endoscopic tubular retractors. 67% remove "as much disc as possible", while 32% remove "ONLY herniated part". In the case of dural tears, 78% of respondents use fibrin glue (Tisseel). Prior to closure, majority of neurosurgeons do NOT use a fat graft (79%) or epidural steroids (65%). With respect to discharge from the hospital, 63% on next day, 21% on same day, and 16% in two days. Return to work is not recommended until at least 6 weeks post-op (97%). Most neurosurgeons (94%) would not operate on an individual with a chief complaint of low back pain. *Conclusions:* Our survey has identified variations in practice patterns amongst Canadian Neurosurgeons with respect to performing one-level lumbar discectomy. This survey is expected to form a basis for the design of a randomized controlled trial in the evaluation of the best management approach for this common procedure.

P-109

Thoracic arachnoid cyst with spinal cord herniation through a ventral dural defect: case report

T Darsaut (Edmonton), R Fox (Edmonton)*

Objective: We report a case of a 53 year old man with a thoracic arachnoid cyst with progressive myelopathy and herniation of the spinal cord through a ventral dural defect. *Clinical Presentation:* The patient had been diagnosed with Charcot-Marie-Tooth Type 1A four years prior, and had experienced slowly progressive loss of sensation and strength in his distal extremities. Subsequent deterioration in strength of his proximal lower extremities, along with the development of urinary retention and fecal incontinence led to an MRI of the thoracic spine. This demonstrated a dorsal arachnoid cyst at the T3-T4 level, with marked spinal cord deformation. The MRI also suggested possible spinal cord herniation anteriorly. *Intervention:* The patient underwent a two level thoracic laminectomy for exploration and fenestration of the arachnoid cyst. At surgery, the spinal cord was found to be herniated through a ventral dural defect. This was reduced and the defect patched using synthetic allograft. Post-operatively, proximal lower

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extremity strength was improved. *Conclusion:* Spinal cord herniation is a rare but increasingly recognized entity that should be considered in the differential diagnosis of a progressive myelopathy.

P-110

In vitro study of traumatic loading after implanting the Bryan cervical disc prosthesis.

N Duggal (London), N Crawford (Phoenix), R Chamberlain (Phoenix), S Baek (Phoenix)*

Background: Insertion of the Bryan cervical disc prosthesis requires resection of the stabilizing disc and ligaments. To explore the potential susceptibility of the cervical spine in the setting of trauma, we studied load to failure in human cadaveric specimens implanted with Bryan disc prostheses. *Methods:* Fifteen cervical spine segments (C3-T1) were implanted with appropriately sized Bryan disc prostheses at C5-6. Using pure moments, 5 specimens were loaded to failure in flexion, 5 in extension, and 5 in axial rotation at a constant cable uptake rate corresponding to approximately 0.5 degrees per second. *Results:* Specimens failed at loads of 9.4 ± 3.2 Nm (mean ± standard deviation) in flexion, 6.2 ± 1.3 Nm in extension, and 11.0 ± 1.7 Nm in axial rotation. The load required for failure during axial rotation was statistically significantly greater than the load required for failure during extension (p=0.04, Kruskal-Wallis one-way analysis of variance on ranks followed by Dunn's method). Other pairwise comparisons were not significant. *Conclusions:* In all three loading modes, the magnitude of loading to induce failure exceeded the ranges commonly considered physiological, implying that implantation of the Bryan disc does not render the spine acutely unstable

P-111

Isolated intramedullary non-caseating granulomatous mass of the conus medullaris

E Frangou (Saskatoon), M Kelly (Saskatoon), S Hattingh (Saskatoon), C Robinson (Saskatoon)*

Background: Sarcoidosis and tuberculosis are multi-system granulomatous diseases that can affect any part of the nervous system. However, very few reported cases exist of a non-caseating granulomatous mass affecting the conus medullaris of the spinal cord. *Methods:* A previously healthy 29-year-old male presented with a one year history of progressive right-sided foot drop. The remainder of his neurological examination was normal. Chest X-ray was normal but a tuberculin skin test was positive. Magnetic resonance imaging (MRI) showed an intramedullary conus medullaris mass. *Results:* The patient had gross total resection of the intramedullary conus medullaris lesion. Pathological examination revealed non-caseating granulomatous inflammation without evidence of microorganisms on culture. PCR of the specimen was negative for Mycobacterium tuberculosis. Although tuberculosis could not be demonstrated outside of his positive skin test, the patient was placed on three antituberculous medications for 1 year. No recurrence was observed on MRI at one-year follow-up. He remained neurologically unchanged with a persistent foot drop. *Conclusion:* Granulomatous lesions of the conus medullaris are exceedingly rare and may present a diagnostic dilemma. We review the available literature on neurosarcoidosis and neurotuberculosis in the context of this patient s unusual presentation.

P-112

Anemia after traumatic cervical spinal cord injury: Evidence for dysregulation of autonomic control based on a clinical and histomorphometric examination of a human spinal cord database

J Furlan (Toronto), M Fehlings (Toronto)*

Background: Since the autonomic nervous system extensively innervates hematopoietic organs, we hypothesized that destruction of descending vasomotor pathways (DVPs) may be associated with anemia after acute cervical spinal cord injury (SCI). *Methods:* This study included a retrospective cohort analysis and a histopathological/molecular analysis of human SCI tissue. *Results:* We examined the data of 24 consecutive SCI individuals (7F,17M, ages 17-83years) admitted from 1998-2000 and 11 matched controls (5F,6M, ages 18-75years). Anemia was significantly more frequent 1-week post-SCI (91.7%) than in controls (25%). Mean hemoglobin concentration (Hb) after SCI was unaffected by age (R=0.824; p=0.357); however, a lower Hb was associated with severe SCI (p=0.003) and female gender (p<0.001). Mean fluid balance within the first week post-SCI was similar in both patient groups (p=0.892). Postmortem spinal cord sections below the injury site from 4 men with severe cervical SCI (ages 66-82years) and from 3 uninjured men (ages 30-73years) were quantitatively examined for myelin (LFB) and for axons (NF200). Anemia occurred in all SCI cases at one-week post-injury. Mean Hb was inversely correlated with the number of preserved axons within DVPs (R=828; p=0.028). There was a trend for an inverse correlation between the extent of degeneration and Hb (p=0.077). *Conclusions:* Anemia is frequent and correlates with the extent of injury. Our data suggest that destruction of DVPs may play important role in the pathobiology of anemia after acute cervical SCI.

P-113

The degree of leukocytosis during the first week after injury is predictive of outcome in patients with acute cervical traumatic spinal cord injury (SCI)

J Furlan (Toronto), M Fehlings (Toronto)*

Background: While clinical evidence indicates that leukocytosis in brain injury is associated with injury severity and neurological outcome, the role of blood leukocyte count (BLC) in SCI recovery received a little attention. *Methods:* This retrospective cohort study included all consecutive individuals with cervical SCI and control cases with spine trauma and no neurological deficit who were admitted between 1998-2000. We excluded cases with polytrauma, systemic diseases and diabetes. *Results:* There were 21 SCI individuals (6F,15M, ages 17-83years) and 11 matched controls (5F,6M, ages 18-75years). Leukocytosis (BLC>11x109/L) was significantly more frequent in SCI individuals (61.9%) than controls (18.2%). The mean BLC was also higher 1-week post-SCI than in controls (p=0.04). Using multiple linear regression, we found no significant correlation of mean BLC with age (R=0.181;p=0.604), gender (p=0.893), injury severity (p=0.93) and level of SCI (p=0.87). Using multiple logistic regression, the neurological

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improvement was correlated with the mean BLC within the first week post-injury (p=0.054) and the severity of SCI (p=0.034), but not with corticosteroid therapy (p=0.149). Also, development of leukocytosis at one week post-injury was not correlated with the severity of SCI (p=0.212) or corticosteroid therapy (p=0.595). *Conclusions:* Leukocytosis is a frequent hematological change during the early stage of SCI. Regardless of potential corticosteroid effects the mean BLC at one week post-injury appears to be a reliable predictor of neurological recovery following SCI.

P-114

A practical classification of spinal cord cavernous malformations

*A Hasan * (Montreal), D Sirhan (Montreal), G Bertrand (Montreal)*

Body of Abstract *Background:* Spinal Cord Cavernous Malformations (SCCM) are considered rare. Only 180 cases (ours included) have been reported to date (1903-2004). *Methods:* This is a review of nine cases of SCCM that presented to our institution. Multiple characteristics of our cases were studied: duration of clinical history; symptoms; site; size; associated venous anomalies; presence of syrinx; postoperative outcomes & follow up. *Results:* We will propose a classification based on clinical presentation (acute hemorrhagic, event based and clinically progressive) and structural characteristics (deep, subpial & exophytic). The number of patients in our study under our classification scheme is: - clinical presentation (4 deep, 3 subpial and 2 exophytic) & structural (2 acute hemorrhagic, 2 event based and 5 clinically progressive). *Conclusions:* This classification will assist in future management, prognosis of SCCM and will serve as a platform for future retrospective and prospective studies.

P-115

Antiproliferative activity of liposomal doxorubicin and Oxaliplatin in malignant glioma cell lines

Annie Larouche (Sherbrooke), Fernand Gobeil (Sherbrooke), David Fortin (Sherbrooke)*

Malignant astrocytomas are aggressive tumors of the central nervous system. Standard chemotherapy, usually following surgery and radiotherapy, offers a minimal survival advantage to the patients. Research in neuro-oncology is very active, and new combinations of chemotherapy that would improve significantly the survival of these patients is constantly sought. Doxorubicin has already been shown to be one of the most active chemotherapy agents in different glioma cell lines. Platinum coumpound are also active against glioma cell lines. We hereby describe a new combination of chemotherapy that presented promising results in our laboratory against malignant glioma cell lines. We investigated individually, and in combination the agent Caelyx, a liposomal formulation of doxorubicin, and the agent oxaliplatin, a recently designed platinum compound. The essays were performed on F98 and the U-118 cell lines. Specifically, we investigated the effects of these drugs on cytotoxicity and cell proliferation, using cell count and MTT essay for cytotoxicity, and WST-1 essay for proliferation. The Caelyx was the more active agent, with significant growth arrest at 24, 48 and 72 hours after a 6 hours exposition. However, the combination of both was synergistic in producing growth arrest, and the cytostatic effect was maintained at 72 hours.

P-116

Treatment with minocycline reduces neuronal loss and apoptosis after spinal cord injury in mice

H Li (Calgary), J Wells (Calgary), J Hurlbert (Calgary), S Casha (Calgary), VW Yong (Calgary)*

Traumatic spinal cord injury produces permanent neurologic deficits due to the primary mechanical insult and subsequent secondary degenerative responses. We have previously reported that minocycline improves functional recovery from spinal cord injury in mice (Wells et al., Brain 126:1628-1637, 2003), but whether this involved neuroprotective mechanisms such as the attenuation of neuronal death was not investigated. In the current study, we have tested the hypothesis that minocycline reduces neuronal cell death after spinal cord injury. Adult mice were subjected to a spinal cord compression injury at the level of T3-4, and were treated with minocycline (50 mg/kg) or saline beginning 1 hour after injury. Subsequent injections were also given. The mice were allowed to survive for 2 or 5 days. Longitudinal sections of spinal cords were processed for NeuN and TUNEL stains. Minocycline treatment significantly reduced neuronal loss in both the epicenter and adjacent areas of spinal cord injury. In addition, the animals receiving minocycline for 5 days exhibited fewer TUNEL-positive cells compared to vehicle-treated controls. These data suggest that minocycline treatment is neuroprotective after spinal cord injury in part by reducing neuronal loss. Minocycline may be an effective therapy after acute spinal cord injury in humans.

P-117

Spinal cord herniation: -a rare cause of thoracic myelopathy. A case report.

K MacDougall (London), N Duggal (London), D Lee (London)*

Background: Idiopathic spinal cord herniation is a rare condition that can present with myelopathy. *Methods:* We report a case of a spinal cord herniation in a 57 year old gentleman who presented with a five year history of progressive leg weakness, pain, and urinary urgency. *Results:* MRI of the spine demonstrated a ventral dural spinal cord herniation at T4/5 with evidence of an atrophic cord and displacement to the left. Using a three level lamminectomy centred at T4 and a left transpedicular approach at T5, we were able to facilitate a left paramedian durotomy. This was performed to minimize spinal cord retraction. A large segment of the ventral spinal cord had herniated through the defect and had a gliotic, exophytic appearance. Using gentle cord retraction we were able to occlude the dural defect with a fat graft. Cadaveric fascia lata was used to reconstruct the thecal sac at this level. A primary repair of the dural defect was not performed. *Conclusions:* Experience with idiopathic spinal cord herniation is small and its pathogenesis remains unclear. To avoid spinal cord retraction, we propose thecal sec reconstruction with cadaveric fascia instead of primary repair of the dural defect.

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P-118

Paraspinal tumors

Ramez Malak (Montreal), Robert Moumdjian (Montreal)*

Abstract: *Background:* Dumbbell tumors are rare tumors of the spinal cord that represent a formidable challenge to the neurosurgeon because they have both intra and extra spinal components. *Methods:* We present a retrospective study of our experience with dumbbell tumors (cervical, thoracic, and abdomio-pelvic) in the last ten years, at the Notre Dame Hospital. Only tumors that had Para spinal components were included in this study. We analyzed the presentation, associated conditions (especially skin and ocular stigmas of neurofibromatosis), investigations, surgical approach, pathological findings, and follow up. *Results:* 17 patients were operated for dumbbell tumors by five neurosurgeons, assisted by ENT, orthopedic, thoracic, general, and plastic surgeons. 5 had cervical, 7 had thoracic, and 5 had abdomino-pelvic tumors. The histology was mainly schwannoma, 1 melanotic schwannoma, 1 neuroenteric cyst, 1 angiomyolipoma, and 3 neurofibromas. Different approaches were used: posterior, anterior, extracavitary, thoracotomy, and retroperitoneal. Complete tumor resection was possible except in two patients. No major complications were found in a follow up of 2 to 40 months. *Conclusions:* Dumbbell tumors of the spinal cord are complex and versatile tumors that need careful planification and a team work with other specialists. The neurosurgeon should be flexible and have different approaches depending on the location and the spatial organization of the tumor. Only symptomatic, and fast growing tumors should be operated.

P-119

Treatment of spasticity with intrathecal baclofen administration

S Mittal (Montreal), J-. Farmer (Montreal)*

Background: Baclofen is a powerful muscle relaxant and antispasmodic agent and has been widely used since the early 1970s to treat spasticity. Intrathecal baclofen was first introduced in the treatment of spasticity by Penn and Kroin in 1984. *Methods:* The medical records of 40 patients who underwent intrathecal baclofen pump placement for the treatment of severe chronic spasticity were reviewed. *Results:* The average age at surgery was 10.3 years (range = 3.9 to 19.7). The average follow-up period was 1.9 years (3 months to 6.4 years). All had a beneficial effect to intrathecal baclofen by day 4 and all patients showed a significant reduction of spasticity. The mean dosage of baclofen was 284 µg/day (range = 75 to 2000). Patients with predominant dystonia required a significantly higher infusion rate (mean = 992 µg/day) compared with children with predominant spasticity (mean = 162 µg/day). *Conclusions:* Intrathecally administered baclofen is effective in reducing the manifestations of spasticity including tone, spasms, and reflex activity. Complications are relatively frequent and mostly related to hardware failure.

P-120

Multimodality intraoperative neurophysiological monitoring findings during surgery for adult tethered cord syndrome: a prospective evaluation in a consecutive series of 44 cases

G Paradiso (Toronto), G Lee (Toronto), R Sarjeant (Toronto), L Hoang (Toronto), M Fehlings (Toronto)*

Background: During microsurgery for adult tethered cord syndrome (TCS), the conus medullaris and roots are exposed to potential injury. Multimodality intraoperative monitoring (IOM) has been used to prevent damage; however its role has not been previously assessed in detail. *Methods:* IOM was performed during de-tethering procedures in 44 consecutive adult patients. Posterior tibial nerve somatosensory evoked potentials (SEP) and EMG of leg muscles, anal and urethral sphincters, were continuously monitored. Electrical stimulation was applied to the filum terminale and structures suspected of carrying neural elements. *Results:* Tethering lesions included tight filum terminale (n=22), post-myelomeningocele repair (n=9), lipomyelomeningocele/lipoma (n=6), split cord malformation (n=4) and arachnoidal adhesions (n=3). Postoperatively, two patients with severe arachnoidal adhesions related to previous surgery developed new neurological deficits. One of these patients showed significant SEP amplitude reduction. Both patients developed EMG bursts. Bursts were recorded in 36 patients, in 8 of these before surgical manipulation. In one patient, low intensity stimulation of the filum terminale elicited sphincter responses, identifying S2-S3 roots that were attached to the filum. *Conclusions:* Multimodality IOM is a useful adjunct to adult TCS microsurgery. SEPs predict of new neurological deficits with high specificity but low sensitivity. Continuous EMG recording is highly sensitive, but false positives may be common. Evoked EMG, including recording from both the anal and urethral sphincters, is a critical intraoperative adjunct which influences the microsurgical approach in over 50% of cases in our hands.

P-121

Transplantation of adult rat spinal cord ependymal region precursor cells into the injured adult rat spinal cord

A Parr (Toronto), I Kulbatski (Toronto), C Tator (Toronto)*

Background: Precursor cells are self-renewing and multipotential. Transplantation of these cells may help to repair the injured spinal cord, however the optimal cell type, transplantation site, and time of transplantation are not well established, nor is the cellular fate. *Methods:* Spinal cord precursor cells were harvested and cultured from adult male Wistar rats expressing enhanced green fluorescent protein. Neurospheres were transplanted at the time of clip compression injury (35g force) into the injury site or 1mm rostral and caudal to the injury site. The optimal site of injection was then utilized to transplant neurospheres in a delayed fashion at 9 and 28 days post-injury. Rats were sacrificed at 7, 14, and 28 days after transplantation. Immunohistochemistry was performed to determine cellular fate. *Results:* Live transplanted cells were identified in the injured adult rat spinal cord at 28 days after injury. Cell survival was improved in rats receiving rostral and caudal injections. Studies of the effects of delayed transplantation are ongoing. *Conclusions:* Adult rat spinal cord precursor cells transplanted into the injured

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adult rat spinal cord survive and differentiate for 28 days. Survival is improved with injection rostral and caudal to the injury site. Cellular differentiation and the effects of delayed transplantation will be discussed.

P-122

Long-term radiographic results in treatment of cervical spondylotic myelopathy: posterior decompression and screw-rod stabilization does not worsen pre-existing global cervical kyphosis

G Pickett (Manchester), K Das (New York), N Duggal (London)*

Background: Anterior cervical decompression and fusion is the recommended surgical approach to cervical spondylotic myelopathy if cervical kyphosis is present. However, multi-level anterior procedures have higher rates of complications and nonunion. In patients with multi-level compression, laminectomy with lateral mass instrumentation may relieve neurological symptoms without substantially worsening cervical alignment. *Methods:* We retrospectively reviewed radiographic and clinical outcomes on 28 patients with cervical spondylotic myelopathy who underwent posterior cervical laminectomy with fusion and lateral mass screw instrumentation. *Results:* Mean patient age was 65 years (range 44-81). Laminectomy of C3-7 was most commonly performed (mean number of levels 4.4.) The mean preoperative C2-7 Cobb angle was -5.8 degrees (range -22 to 11), with all but 2 patients having a straight or kyphotic cervical spine. Surgical correction of kyphosis was obtained in 2 cases. Immediately post-operatively, the mean C2-7 angle was -5.2 degrees. Follow-up to 26 months showed no significant progression of cervical kyphosis, with a mean C2-7 angle of -5.0 degrees in most recent follow-up (P = 0.30, paired student t-test). All patients obtained solid arthrodesis and improvement in neurological symptoms. *Conclusion:* Posterior cervical laminectomy with lateral mass instrumentation is a reasonable option for multi-level cervical decompression, even in patients with straight or kyphotic spines preoperatively.

P-123

Early complications with cervical arthroplasty

G Pickett (Manchester), L Sekhon (Sydney), W Sears (Sydney), N Duggal (London)*

Background: While cervical arthroplasty for the treatment of degenerative disease may offer benefits over arthrodesis, it also requires the acquisition of new operative techniques, and introduces new potential complications. *Methods:* We prospectively recorded operative data, complications, clinical and radiographic outcomes in all patients who received the Bryan® artificial cervical disc in two tertiary care centers since 2001. Patients underwent standard anterior cervical discectomy followed by arthroplasty at one to three levels. *Results:* Ninety-six discs were implanted in 74 patients. One patient developed a retropharyngeal hematoma requiring evacuation. Neurological worsening occurred in 3 patients. Intraoperative migration of the prosthesis was observed in one bi-level case, while delayed migration occurred in one patient with post-operative segmental kyphosis. Another patient with severe segmental kyphosis required revision with a custom lordotic prosthesis. Heterotopic ossification and fusion occurred in 2 cases; motion was preserved in the remaining 94 prostheses. Partial dislocation of the prosthesis in extension developed in one patient with preoperative segmental hypermobility. Twenty-five percent of patients reported neck and shoulder pain in late follow-up. There was a trend towards increased kyphosis of the C2-7 curvature post-operatively. *Conclusion:* The Bryan® disc prosthesis was effective in maintaining spinal motion. Major perioperative and device-related complications were infrequent.

P-124

Cervical syrinx presenting with acute and episodic symptoms resembling transient ischemic attack

Z Siddiqi (Edmonton), M Sawa (Edmonton), S Ahmed (Edmonton)*

Introduction: Syringomyelia is a chronic and progressive condition that usually manifests as muscle weakness and dissociated sensory loss in affected myodermatomes. *Case Report:* A 31-year old previously healthy pastor presented with eight month history of episodic numbness and weakness of the right shoulder and arm, particularly during strenuous workouts. He would be unable to lift his arm against gravity and the whole arm would feel "dead" with a poorly localized pain. Symptoms would resolve completely after few hours. No neck pain or any bowel or bladder disturbance were reported. Examination showed mild weakness in the right biceps and triceps (MRC grade 4+). Sensations over the cervical dermatomes and muscle stretch reflexes were normal. *Results:* Nerve conduction studies in affected arm, including late responses, were normal. Needle EMG studies suggested a multilevel cervical radiculopathy with ongoing denervation. C-spine MRI showed a 2 x 0.4cm syrinx at the C6-7 level with a normal cervicomedullary junction. CSF studies, C-spine x-rays and brain MRI were normal. Since initial evaluation our patient has had three episodes of urinary incontinence and is currently awaiting neurosurgical evaluation. *Conclusion:* Our case illustrates an unusual presentation for syringomyelia. It is likely that increase in CSF pressure within the syrinx during exercise may have lead to transient symptoms.

P-125

Routine histopathological examination of intervertebral disc specimens: a cost-benefit analysis

A Wu (Saskatoon), D Fourney (Saskatoon)*

Background: The routine histopathological examination of discectomy specimens remains common practice in many Canadian hospitals, although it rarely detects clinically significant unsuspected disease. *Methods:* A database analysis identified 1320 patients with disc specimens evaluated at Royal University Hospital between 1996 and 2004. Procedure and diagnostic codes were used to classify cases as "routine" and "nonroutine" (the latter including trauma, tumor, infection and major deformity cases). An unusual pathological diagnosis prompted a chart review to determine whether the findings were expected based on clinical or imaging data. Cost-benefit values were calculated. *Results:* We excluded 11 cases with incomplete records. There were 1266 normal disc specimens: 967 were obtained during routine procedures and 299 from nonroutine procedures. Unusual pathology was seen in 43 cases: 39 were from nonroutine procedures where the results were expected. There were 4 routine cases with unexpected pathology,

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including deposits of calcium pyrophosphate crystals (3 cases) and amyloid (1 case). None resulted in a clinical diagnosis, although the patient with amyloidosis was screened for multiple myeloma. The cost per case of identifying a significant pathological diagnosis was $17,107 in routine cases, and $610 in nonroutine cases. *Conclusion:* In routine cases, histopathological examination of disc specimens is not justified.

PEDIATRICS

P-126

Risk factors for carbamazepine induced leucopenia in children.

AliAkbar Asadi-Pooya (Shiraz)*

Background: Carbamazepine (CBZ) is a commonly used anticonvulsant agent, but it has been linked with different blood cell abnormalities. I tried to determine some of the risk factors associated with CBZ induced leucopenia in Children. *Methods:* This nested-cohort study was conducted on 41 children with epilepsy who received CBZ monotherapy. From all of the patients, baseline blood tests were obtained before starting medication and then serially. The patients were followed for at least one year. *Results:* Totally, 13 patients (31.7%) developed leucopenia in follow up blood tests. Four factors were observed to be associated with CBZ induced leucopenia. The first factor was sex; as leucopenia was more common among girls (P = 0.018). The other factors were lower white blood cell (WBC), neutrophil and monocyte counts in the first complete blood count (CBC). *Conclusion:* It is very important to have a CBC in everyone, before treatment with CBZ is started. After that, the frequency of blood monitoring can be determined on an individual basis. It is reasonable to be very careful and follow the patient repeatedly and closely when deciding to start CBZ in a girl with borderline low WBC, neutrophil or monocyte count.

P-127

Health related quality of life in children with cerebral palsy

C Campbell (London), P Humphreys (Ottawa), J McLean (Ottawa), R Nair (Ottawa)*

Background: Despite the major impact of Cerebral Palsy (CP) on a child and their caregivers little data has accumulated on Health Related Quality of Life in children with CP. Only one specific HRQL measure has been developed and few generic instruments have been applied to this population. *Methods:* Children age 2 to 15 years with CP followed at the Ottawa Children's Treatment Centre or the Children's Hospital of Eastern Ontario were enrolled in a larger cross-sectional study examining bone health. CP was classified using the Gross Motor Function Classification System (GMFCS). Three measures of HRQL were administered: the Health Utilities Index (HUI) II and III (generic), as well as the Caregiver Questionnaire (CQ) (disease specific). During an investigator led interview measures were completed by a parent/guardian proxy. Comparative data were taken from the Ontario Child Health Survey (OCHS). *Results:* Forty-six subjects were included. Ages ranged from 2.5 to 15.8 years (mean= 9.1). Forty-four percent of the sample was in GMFCS levels 4 or 5. HUI utility scores ranged from negative 0.34 to 1.00 with a mean of 0.309, substantially different from children in the OCHS. CQ scores ranged from 0.1 to 7.1. Pearson correlations between the HUI and CQ total scores were strongly correlated (negative 0.744, p less than 0.001). HRQL scores were poorer with increasing severity of CP. Mean HUI III scores were 0.706 and negative 0.202 for GMFCS level 1 and 5, respectively. *Conclusions:* Parent reported HRQL is significantly compromised in this sample of children with CP. As a disease specific measure of HRQL the CQ corresponds well to an established generic measure in children with CP.

P-128

National activity profile of Canadian adolescents with migraine

J Dooley (Halifax), K Gordon (Halifax), E Wood (Halifax), P Brna (Halifax)*

Objective: As migraine is reportedly associated with harm avoidance, we hypothesized that Canadian adolescents with and without migraine would have different exercise patterns. *Methods:* We analysed data from the Canadian Community Health Survey, Cycle 1.1 (2000-2001). 6470 respondents aged 12-14 years and 11079 aged 15-19 years reported whether they had "migraine headaches diagnosed by a health professional". Respondents were subsequently asked "Have you done any of the following in the past 3 months?" with a sequence of 20 specified exercise patterns. Data were analyzed using Systat v9.0 and Stata/SE 7.0. Analysis used Logistic regression and ANOVA with age and gender included to adjust for the association of age and sex with exercise patterns. A response regarding migraine was reported by 99.9%. Missing or not applicable data was unavailable for 12.9% of all respondents for all exercise data. *Results:* Adolescents with migraine are as likely as their peers to participate in contact sports, such as ice hockey, basketball, downhill skiing and snowboarding. They were more likely to be active on a daily basis (p=0.03), for >15 minutes (p<0.001) and to expend more energy in activity (p<0.001). Activities favoured by adolescents with migraine over their peers without migraine included: walking (p<0.0001), gardening and yard work (p=0.008), popular/social dance (p=0.02), jogging (p=0.002), baseball (p=0.012) and fishing (p=0.025). *Conclusions:* Canadian adolescents with migraine are as likely to play contact sports as their peers who do not have migraine. They report more daily activity and are more likely to be involved in non-contact activities.

P-129

Young Woman Who Beat Medication Induced Headache in Two Weeks

Qais Ghanem (Ottawa)*

This is one of thousands of patients who successfully get rid of their chronic daily headaches, and medication induced headache. The reason I present this is that this a 14 minute video interview of a young woman who happens to be a nurse, describing in detail how she went through the process, including her skepticism, her fears and experience and describing what factors in her interaction with her neurologist made her go through with it. It is a dramatic success story, captured on film. I feel that it would be of help to younger newly qualified neurologists who read about the treatment but have their own doubts. Many years ago I wished I had the opportunity to

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view such film. It should also be very effective, to persuade other patients to withdraw analgesics and succeed, if given the film to watch.

P-130

Is migraine a risk factor for the development of concussion?

K Gordon (Halifax), J Dooley (Halifax), E Wood (Halifax)*

Objective: To explore a clinical impression that a history of migraine is reported more frequently in adolescents with sport related concussion. *Methods:* We analysed data from the Canadian Community Health Survey, Cycle 1.1 (2000-2001). 25,141 respondents, aged 12-24 years reported whether they had "any injuries that were serious enough to limit their normal activities" in the preceding 12 months and the nature of the most serious injury. Concussions were coded along with internal injuries. They reported whether they had "migraine headaches diagnosed by a health professional" and their exercise activities "of the past 3 months" from a sequence of 20 specified activities. Data were analysed using Stata/SE 7.0. Weights were recoded to reflect the sample size. All exercise activities were screened for association with concussion and entered into a logistic regression model along with age, sex and migraine status. The final logistic regression used 89.6% of the complete data set. *Results:* Logistic regression modeled the following risk factors as significant: migraine (OR 2.1, 95% CI: 1.2, 4.0, p=0.016), male (OR 2.3 95% CI: 1.4, 3.7, p=0.001), playing hockey (OR 2.3, 95% CI: 1.5, 3.8, p<0.001), jogging or running (OR 1.6, 95% CI: 1.0, 2.3, p=0.029), and weight training (OR 1.9, 95% CI: 1.2, 2.9, p=0.003). At least 72% of all concussions were related to sport or physical exercise/leisure or hobby (95% CI: 64%, 82%). *Conclusions:* In this exploratory analysis, migraine appears to be an independent risk factor for concussion. Within this model running and weight training may be proxy variables for other competitive athletics. The association of migraine and concussion requires confirmation using a more rigorous epidemiological study design.

P-131

Concussions in Canada: Descriptive epidemiology:

K Gordon (Halifax), J Dooley (Halifax), E Wood (Halifax)*

Objective: To describe the epidemiology of reported concussion derived from a large, nationally representative health survey. *Methods:* We analyzed the microdata files of the Canadian National Population Health Survey (NPHS: 1996-1997). 81,804 respondents representing 28,606,100 Canadians reported whether they had "any injuries that were serious enough to limit their normal activities" in the preceding 12 months and the nature of the most serious injury. Those reporting concussions were compared to those reporting other injuries and/or the non-injured. *Results:* 99.8% of 81,804 eligible respondents reported their injury experience within the preceding year, with 98 reporting a concussion. The annual incidence of Canadians reporting a concussion as their most serious injury was 110 per 100,000 population (95% CI: 90, 140). Those reporting concussion were more likely to be younger (32% under 15y, 76% under 35y) (p<0.0001) and male (62%) (p<0.0001). Males were significantly over represented in the 16-34y group (OR=4.6, p=0.001). At least 54% of all concussions were sport-related (95% CI: 39%, 67%), occurring at a place for recreation or sport, with sport having a role in 85% of concussions in the 16-34y group (OR=13.1, p<=.0001). Other locations included home (23%), school (7%), and street/highway (4%). Those reporting concussion were more likely to report "excellent" health (p<.001) and higher daily energy expenditure (p<.0001), than those not reporting concussion. *Conclusions:* We present annual incidence estimates of reported concussion, derived from a sizeable nationally representative population survey.

P-132

Pediatric Neurology Ukraine Problems and Potential for improvement.

Volodymyr Kharytonov (Kiev)*

After independence Ukraine started to implement changes in the Health Care System it had inherited from the USSR. It was obvious that the system was isolated and not financially self-sufficient. This led to a deterioration of medical science and the quality of Health Care services. All attempts to change the situation have been thwarted by the worsening economic situation of the country. However, in the last decade a number of improvements have been made in the quality of pediatric neurology services. Foremost of these are: 1. Improving the level of training, certification and credentials for pediatric neurology. 2. Improving the quality and accuracy of diagnostic testing (e.g.. with availability of new technology). Currently, our Health Care service challenges are: 1. An over production of poorly trained physicians, 2. An over supply of hospital beds due to a heavy emphasis on inpatient management, 3. Polypharmacy being widespread yet unaffordable, 4. Poor access to the world medical literature (improving as more and more physicians learn English and have access to the internet). The "Orange" revolution rises our hope in new modern Health Care System that is coming.

P-133

Quality of life and satisfaction among Calgary pediatric neurosciences patients

C Lee (Kingston), J Mah (Calgary), K Barlow (Calgary), D Strother (Calgary), M Hamilton (Calgary), L Hamiwka (Calgary), E Wirrell (Calgary), J Latter (Calgary), W Hader (Calgary), T Myles (Calgary)*

Background: This study compared health-related quality of life (HRQL) among pediatric neurosciences patients, and described their caregivers' perception of family-centered care. *Methods:* A cross-sectional survey was conducted on children who attended neurosciences clinics at the Alberta Children's Hospital. Caregivers completed self-administered questionnaires regarding socio-demographic status; their children's neurological illness, functional disability (FIM/WeeFIM), HRQL (PedsQL); and assessment of medical/rehabilitative services (MPOC-20). *Results:* 278 (45%) patients completed the survey, including twenty-three (8%) with brain injury, twenty-nine (10%) with myelomeningocoele, thirty-three (12%) with brain tumor, fifty-eight (21%) with neuromuscular disease, and eighty-nine (32%) with refractory epilepsy. 165 (61%) patients were male, and the mean age was 11 (SD 4.6) years. Their mean PedsQL physical and psychosocial scores were 63.1 (SD 30.8)

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and 65.9 (SD 22.4) respectively. Children with refractory epilepsy had the lowest psychosocial HRQL (p less than 0.001). The majority of caregivers (92%) were satisfied with the medical care. Their mean MPOC scores ranged from 4.0 to 5.4 out of 7.0, with the lowest score seen in the information domain. *Conclusions:* Neurological disorders had a significant impact on pediatric HRQL. Despite satisfaction with care, families perceived a need for more information. Further studies will explore health services utilization among pediatric neurosciences patients.

P-134

Pediatric ruptured intracranial aneurysm associated with undiagnosed aortic coarctation

N McLaughlin (Montreal), MW Bojanowski (Montreal)*

Introduction: Aortic coartation (AC) is associated with an increased frequency of ruptured intracranial aneurysms (IA). Although the diagnosis of congenital heart disease rarely precedes the cerebrovascular complications, its recognition following aneurysmal subarachnoid hemorrhage (SAH) is important for peri-operative management. *Method:* Case report. *Results:* A 12 yr-old boy in good health consulted 3 days after the sudden onset of a severe headache with nausea and vomiting. Neurological exam revealed nuchal rigidity. CT scan showed discrete SAH around the left internal carotid artery. Angiography demonstrated a left PcoA aneurysm and severe vasospasm. Thorough examination revealed elevated blood pressure (BP), discrepancy between upper- (190/80) and lower-extremities (68/48) BP, weakness of lower-extremity pulses, systolic heart murmur. Pre-operative echocardiography confirmed the presence of AC. Intra-operatively, renal and lower extremities perfusion were closely monitored. Post-operative day 1, symptomatic VS developed and treated with balloon angioplasty and verapamil intra-arterial infusion. Since no clinical improvement occurred, milrinone intra-arterial injection followed by an IV perfusion were attempted. The patient recovered completely with no systemic ischemic complications . *Conclusion:* The presence of AC should be evoked in young patients presenting with IA. Its recognition is essential for adequate peri-operative and vasospasm management, AC treatment, and prevention of future aneurysm formation.

P-135

Pediatric neurotrauma in Kathmandu, Nepal: implications for injury management and control

K Mukhida (Toronto), M Sharma (Kathmandu), S Shilpakar (Kathmandu)*

Background: There is a scarcity of data regarding childhood neurological injuries in developing countries. The epidemiology of acute pediatric neurological injuries in Nepal was studied to assess the implications of these data for injury prevention programs. *Methods:* The clinical records of patients 18 years of age and younger who presented to Tribhuvan University Teaching Hospital between April 1, 2001 and April 1, 2004 with acute neurological trauma and were subsequently admitted to hospital were retrospectively studied. *Results:* 416 injured children were admitted to hospital. Spinal injuries were relatively rare (4%) compared to head injuries (96%). Falls were the most common cause of injuries (61%). It took significantly longer (p<0.001) for children injured in rural Nepal (62%) to obtain neurosurgical care (30.1 hours) than those injured within Kathmandu (7.1 hours). A Glasgow Outcome Score of 5 was obtained for 96%, 76%, and 22% of patients with mild, moderate, or severe head injuries, respectively. *Conclusions:* Preventive measures for injuries that are applicable to the Nepalese scenario are urgently needed. Interventions should focus on health education programs and upgrading of road safety measures. Neurological injuries must also be viewed in the context of the broader social issues in Nepal that contribute to injury.

P-136

Nutritional combination therapy provides primary benefit and complements corticosteroid intervention in the mdx mouse

Eric Payne (Calgary), Nobuo Yasuda (Hamilton), Jacqueline Bourgeois (Hamilton), Michaela Devries (Hamilton), Christine Rodriguez (Hamilton), Junaid Yousuf (Hamilton), Mark Tarnopolsky (Hamilton)*

Background: There is no cure for Duchenne muscular dystrophy (DMD), and the current long-term corticosteroid therapy is associated with significant side effects. The exercising mdx mouse is a murine model of DMD used to pre-screen experimental therapies. *Methods:* We evaluated four nutritional compounds alone and in combination in the exercising mdx mouse for potential therapeutic benefit: creatine monohydrate; conjugated linoleic acid; alpha-lipoic acid; and beta-hydroxy-beta-methylbutyrate. We also assessed the effectiveness of prednisolone alone, and as an adjunct to the four-compound therapy. Outcome measures included grip strength, rotarod performance, serum creatine kinase levels, muscle metabolite stores, internalized myonuclei, and retroperitoneal fat pad weight. *Results:* In isolation, each treatment demonstrated varying significant therapeutic improvements, while the four compounds in combination conferred more robust benefits. However, prednisolone and the combination therapy administered together provided the most consistent efficacy of any treatment group; improving peak grip strength (P less than 0.01), and decreasing grip strength fatigue (P less than 0.01), the number of internalized myonuclei (P less than 0.01), and the retroperitoneal fat pad stores (P less than 0.001). *Conclusions:* This study provided evidence that the four-compound combination therapy alone, and in conjunction with corticosteroids, is therapeutically beneficial in the mdx model of DMD.

P-137

Saccadic adaptation in Chiari type II malformation

M Salman (Winnipeg), J Sharpe (Toronto), M Eizenman (Toronto), L Lillakas (Toronto), T To (Toronto), C Westall (Toronto), M Steinbach (Toronto), M Dennis (Toronto)*

Background: Saccadic adaptation corrects the amplitude of saccades in response to visual errors. Saccadic adaptation is a form of motor learning. The cerebellum is a major participant. Chiari type II malformation (CII) is a developmental deformity of the hindbrain. We investigated the effects of CII on saccadic adaptation, and correlated them with planimetric MRI features of CII. *Methods:* We recorded saccades using an infrared eye tracker (El-Mar). Saccadic

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adaptation to target hypometria induced by 3o back-steps of 12o horizontal targets was measured in 21 participants with CII, aged 8-19 years. Target back-steps were triggered during initial saccades to the 12o target steps. Midsagittal MRI brain regions were measured in 19 CII participants. Thirty-nine typically developing children served as controls. *Results:* Saccadic adaptation was achieved in 57% of CII participants who had 11.6% mean reduction in saccadic amplitude, and in 67% of control participants, who had a 13.3% mean reduction in saccadic amplitude. The differences between the groups were not significant and adaptation did not correlate with MRI planimetry of the cerebellum. *Conclusion:* Saccadic adaptation occurs in patients with CII. This indicates intact function of the cerebellar circuits involved in saccadic adaptation despite the deformity of CII.

P-138

Saccade characteristics in children

M Salman (Winnipeg), J Sharpe (Toronto), M Eizenman (Toronto), L Lillakas (Toronto), C Westall (Toronto), T To (Toronto), M Dennis (Toronto), M Steinbach (Toronto)*

Background: Saccades are fast orienting eye movements that are necessary for optimal visual function. Saccadic characteristics have not been measured systematically in a large cohort of children. *Methods:* We recorded saccades using an infrared, head-mounted eye tracker in 39 typically developing children, aged 8-19 years and investigated effects of age and gender. Participants made saccades to visual targets that stepped 10º or 15º horizontally and 5º or 10º vertically at unpredictable time intervals. *Results:* Saccadic latency decreased significantly with increasing age, while saccadic amplitude gain and asymptotic peak velocity did not vary with age. Mean saccadic amplitude gains for the different target steps ranged between 0.90 and 0.96, mean latency ranged between 240 and 268 ms, and mean asymptotic peak velocity ranged between 435 and 537 º/s. There was no gender difference in any saccadic parameter. *Conclusion:* Saccadic amplitude gains and peak velocities in children are similar to reported adult values. This implies maturity of the neural circuits responsible for making saccades accurate and fast. Saccadic latency decreases with increasing age as the brain matures.

P-139

Convergence paralysis as an initial manifestation of polyarteritis nodosa: a pediatric case report

J Wylie (London), C Campbell (London), J Pope (London), D Nicolle (London), R Laxer (Toronto)*

Background: Polyarteritis nodosa (PAN) is a rare systemic necrotizing vasculitis of medium sized arteries which has been reported in fewer than 250 children. Central nervous system manifestations occur in up to 40 percent of patients; however, they usually occur late in the course of the disease. *Methods:* Case report and review of the literature. *Results:* We report on a 15 year old girl who presented with an acute onset of diplopia, intermittent headache, and convergence paralysis. The presence of livedo reticularis, hypertension, right plantar neuropathy, left ulnar neuropathy, and a 25 pound weight loss confirmed the diagnosis of PAN. ANCA (p and c) were negative. MRI of her head revealed a 3 mm focus of restricted diffusion just left of midline in the anterior midbrain representing an acute perforator territory infarct. Nerve conductions demonstrated mononeuritis multiplex. The child has responded well to immunosuppressive therapy, antihypertensives and gabapentin for neuropathic pain. *Conclusions:* Convergence paralysis was secondary to a midline midbrain infarct due to the CNS vasculitis of PAN. To our knowledge this has not been previously described in a child. At the time of diagnosis our patient was being treated with minocycline therapy for acne. This provides support to the previously raised concern that PAN can occur as an adverse effect of minocycline therapy.

General Neurology

P-140

Fibrous dysplasia of the skull base presenting with headache and partial third nerve palsy in an adult: case report

F Amoozegar (Ottawa), A Guberman (Ottawa)*

Background: Fibrous dysplasia of the bone is an idiopathic disorder that manifests as a developmental anomaly of bone-forming mesenchyme. In the craniofacial form, bone deformity, visual loss, hearing loss, and bone pain may be seen. Here, we report a case of sphenoid fibrous dysplasia with an unusual presentation in an adult, and review pertinent literature. *Case History:* A previously healthy 32-year old woman presented with an 8-day history of right-occipital and retro-orbital headache, and a 5-day history of right eye ptosis that progressed to complete eye closure and horizontal diplopia. Neuroimaging showed a lesion at the base of the skull invading the sphenoid sinus. *Results:* A biopsy of the lesion indicated sphenoid fibrous dysplasia. The patient's symptoms were alleviated following biopsy. However, the symptoms returned on several other occasions and a repeat MRI showed growth of the lesion. Excisional surgery was performed and the pathology confirmed monostotic fibrous dysplasia (low-grade fibrosarcoma). Following surgery, the patient had radiotherapy with significant resolution of her symptoms. *Conclusions:* Fibrous dysplasia can rarely present acutely in adulthood with headache and cranial nerve involvement. Early diagnosis is important because of the potential for significant morbidity and malignant transformation.

P-141

An open label study to evaluate the effect of topiramate on subject responsiveness to triptans used for symptomatic headache treatment.

W Becker (Calagary), H Hew (Toronto), S Christie (Ottawa), C Binder (Toronto), J Wang (Mississauga), S Ledoux (Montreal)*

Background: Clinical experience indicates that prophylactic migraine treatment may enhance the efficacy of triptan medications used for acute migraine attacks. *Methods:* This 40 patient, open-label, single-arm, multicentre study consisted of a 6-week baseline period on triptan therapy followed by a 16-week adjunctive topiramate treatment period. Subjects meeting IHS criteria signed consent and entered the baseline period. Those with 3 to 12 migraine

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periods per month during baseline continued with adjunctive topiramate treatment. *Results:* 40 subjects entered the adjunctive topiramate period and 21 subjects received at least 12 weeks of treatment. Mean final dose of topiramate was 124 mg per day (range 50 to 200 mg per day) for the intent-to-treat population. The proportion of triptan-treated migraines pain-free 2 hours post triptan did not differ between the two treatment periods. 14 of 21 subjects experienced a decrease in migraine attacks per 28 days with adjunct topiramate treatment compared to baseline. 13 subjects discontinued due to AEs. The most commonly reported events were paraesthesia, fatigue and dizziness. *Conclusion:* The data suggest topiramate may reduce the total number of migraine attacks when used in combination with triptans but did not result in earlier pain-free attainment with the combination treatment.

P-142

Evaluation of chronic pain with functional MRI

E Berger (Montreal)*

Background: fMRI has been found to identify feigned memory impairment. It gives a response in the anterior cingulate (response inhibition), the right superior frontal gyrus, parts of the prefrontal and premotor cortex. It is less prone to give false positives than multichannel recording (polygraph). *Methods:* With fMRI one postulates that neuronal activity is increased when attempts are made at deception. *Results:* The reasoning behind this theory is that it takes more effort to conceal the truth when constructing a lie and this will show up on fMRI. Spence et al (2001) found that reaction time was longer when subjects lied, the difference being about 200ms. Lying caused greater activity in the ventrolateral, prefrontal, the medial prefrontal (anterior cingulate) and premotor corteces bilaterally as well as the left inferior parietal and lateral premotor cortex. *Conclusion:* Although fMRI has advantages in the evaluation of chronic pain (no need for ionizing injection, facility of data acquisition) it is, at the present time, subject to movement artifacts and therefore not as yet a reliable tool to be used in the clinical setting.

P-143

Neurocysticercosis in Canada: still a rare disease?

JG Burneo (London), RS McLachlan (London)*

Background: Neurocysticercosis is caused by the establishment of Taenia solium larvae in the nervous system, after ingestion of eggs shed in human faeces by the adult tapeworm. Often a life-threatening disease, neurocysticercosis is increasingly recognized as a public health problem, not only in developing countries but also in the US; but has never previously been described in the Canadian medical literature. We described the last 10 years of experience in London. *Methods:* A retrospective review of all the diagnosed cases of neurocysticercosis in the London Health Sciences Centre in the last 10 years (1994- 2004) was performed. *Results:* Four patients (all male) were found, mean age was 42.5 (range: 30-56). Three presented with seizures, one with headaches and visual symptoms. Two cases received surgical treatment and three albendazole. All were symptom-free (including seizures) following treatment. All patients emigrated from or traveled to endemic countries for neurocysticercosis. *Conclusions:* The presence of neurocysticercosis in London and surrounding areas is still rare. The existence of serum and CSF testing can avoid surgery performed for diagnosis. The increase rate of immigration warrants a constant epidemiologic surveillance and evaluation of the indexes' families in order to prevent the emergence of this serious public health problem.

P-144

Giant subarachnoid neurocysticercosis

M Bussiere (London), J Burneo (London)*

Background: Patients infected with the larval form of the pork tapeworm, Taenia solium, may develop focal seizures secondary to the formation of intraparenchymal brain cysts. We review a patient with the uncommon presentation of giant subarachnoid cysts and discuss implications for treatment. *Methods:* A 56 year-old Korean man presented with headaches and visual disturbances, consisting of blurry vision and diplopia. Four years previously, he had developed focal seizures and was found on brain imaging to have multiple intraparenchymal cystic lesions, as well as cysts within the interhemispheric fissure. He had been diagnosed with neurocysticercosis and treated with two courses of albendazole and corticosteroids. *Results:* On examination, he had bilateral papilledema without focal neurological signs. An MRI of the brain revealed giant subarachnoid cysts within the sylvian fissure and suprasellar cistern, as well as ring-enhancing intraparenchymal lesions. He was treated with a third course of albendazole and steroids. *Conclusions:* Medical therapy consisting of multiple courses of antihelminthics with steroids, is the indicated treatment for this type of neurocysticercosis. Surgical removal of cysts should be considered only in patients with life-threatening intracranial hypertension despite corticosteroid therapy.

P-145

Neurological manifestations of Porphyria--an unusual case with central and peripheral nervous system involvement

JY Chu (Toronto), JK Chu (Toronto)*

Background: Porphyria is a group of rare inherited metabolic disorder affecting the biosynthesis of heme which can affect multiple organ systems including the central and peripheral nervous system. An unusual case of acute Variegate Porphyria will be presented with detail discussion regarding the clinical, neuroradiological and neurophysiological features. Relevant literature review and management for this interesting condition will be discussed. *Method:* A retrospective case review. *Results:* A 59 years old nurse of Jamaican decent was initially admitted to hospital with progressive stupor and weakness following a brief febrile illness. Relevant past history includes an episode of unexplained confusion and transient stupor 5 years ago. She also has beta Thalasemia minor, IgG lambda benign monoclonal gammopathy, rheumatoid arthritis and essential hypertension. She is a nonsmoker and nondrinker and there is no family history of similar illness. Aside from taking acetaminophen for her fever, she was not on any other medications. Initial examination showed her to be stuporous with Glasgow Coma Score of 8 (3+3+2) with temperature 38.8C, BP was 130/90. There were no localizing neurological findings and she did not have any meningismus. Her general examination showed no skin rash or hepatosplenomegaly. Plain CT brain scan was normal

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but gadolinium enhanced MRI showed non-enhancing T2 lesions in the brainstem and both thalami. CSF showed no pleocytosis but mild elevation of protein of 1.0 G/L (Normal less than 0.60) but was negative for all infective agents including PCR for Herpes virus. Her EEG showed diffuse slowing without any focal abnormality. EMG and NCS demonstrated a severe axonal motor and sensory peripheral neuropathy. Her liver function tests were all normal but her urine for Uroporphyrin I and III, Coproporphyrin I and III were all significantly elevated compatible with a biochemical abnormality as seen in Variegate Porphyria. She received respiratory and general medical supportive care in the Intensive Care Unit and eventually made a complete recovery from this acute Porphyria attack. Follow up EMG and NCS confirmed improvement in sensory and motor electrophysiological parameters. *Conclusions:* Porphyria is a rare metabolic disorder; early recognition of the typical involvement of central and peripheral nervous system would lead to the correct diagnosis and appropriate management. A brief review of the pathophysiological mechanism of Porphyria and its management will be presented.

P-146

Recent experience with adrenoleukodystrophy in adult patients in St. John's, Newfoundland

*M Eustace** (St. John's), M Stefanelli (St. John's), A Goodridge (St. John's), J Barron (St. John's)*

Background: We report two unrelated cases of ALD diagnosed in the past year. *Clincial Presentation:* Case 1: A 44 year old male with a grand mal seizure. He had limited communication ability, impaired gait, anorexia, hyperreflexia, and bilateral Babinski responses. Personality changes started six years prior; he was diagnosed with schizoaffective disorder. He was investigated 18 months prior for spastic gait, hyperreflexia, and language dysfunction with no diagnosis. Case 2: A 31 year old male presented from a long term care facility with urosepsis. Past history included Addison's disease and alcoholism. Bipolar disorder and Wernicke's-Korsakoff's syndrome were diagnosed in 2002 due to personality changes and progressive dementia. Despite abstinence from alcohol, he continued to deteriorate. He was unable to communicate, had increased tone and bilateral Babinski responses. He developed dysphagia requiring PEG tube insertion. *Intervention:* Case 1: MRI revealed white matter changes. Brain biopsy was consistent with ALD. VLCFAs were consistent with ALD. Case 2: MRI revealed bilateral high signal intensity in the cerebellum and the posterior thalamic nucleus extending superiorly to the posterior limb of the internal capsule bilaterally. VLCFAs were consistent with ALD. *Conclusion:* Case 1: Transferred to long term care Case 2: Deceased October 19, 2004

P-147

Delayed presentation of decompression illness may benefit from prolonged hyperbaric treatment

W Fitzpatrick (Saskatoon), R Banner (Saskatoon), J Scott (Saskatoon), C Boyle (Saskatoon)*

Background: All divers are potentially at risk of decompression illness (DCI). Diffuse, multifocal central neurologic abnormalities may occur, with spinal cord white matter being particularly vulnerable. Complete resolution of symptoms is most likely to result from early diagnosis and hyperbaric therapy. *Methods:* Case report. *Results:* A 29 year old male presented ten days after recreational diving with otalgia, pruritis, joint pain, limb paresthesias and urinary retention. He had no history of previous neurological disease. Risk factors for DCI included patent foramen ovale, continued diving after symptom onset and flying after diving. MRI demonstrated T2 hyperintensities at multiple spinal cord levels with enlargement of the conus. Partial clinical recovery occurred following standard hyperbaric treatment, followed by a plateau and then worsening of his neurological symptoms. Near complete clinical and radiological recovery occurred with a prolonged protocol of sixty "tailing" treatments. *Conclusion:* Ideally, DCI should be diagnosed and treated promptly. This case demonstrates that with delayed presentation the patient may require prolonged hyperbaric treatment to achieve clinical recovery.

P-148

Tutoplast Dura graft: association with Creutzfeldt-Jakob disease

R Gervais (Ottawa), R D'Amour (Ottawa), T Sutcliffe (Ottawa), GH Jansen (Ottawa), L Elmgren (Ottawa), G Coleman (Ottawa), A Giulivi (Ottawa)*

Background: Tutoplast Dura, a commercially processed dura mater obtained from human donors, was available in Canada between January 1982 and April 2002. In 2003, Creutzfeldt-Jakob disease (CJD) was confirmed in a 59-year-old patient who had received Tutoplast Dura in 1992 during neurosurgery. *Methods:* The Public Health Agency of Canada, Health Canada, the Provincial Department of Health, the local Public Health and the involved hospital collaborated in the investigation. Hospital records were reviewed. Both the Manufacturer and Canadian distributor were contacted for information on collection and processing of the graft. *Results:* Donors were screened for neurological illnesses and no commingling of dura from different donors occurred during processing. This graft was treated with 0.1 N sodium hydroxide, a less concentrated disinfectant solution than material manufactured after October 1992. The graft was packed in a box which may have contained another graft from the same donor. The donor medical history was not available. Potential recipients of the other graft were notified. *Conclusions:* This is the first reported case of CJD in Canada associated with Tutoplast Dura. Although a definite causal association was not established, health care providers should be aware of the possibility of iatrogenic CJD in recipients of Tutoplast Dura in whom neurological signs and symptoms develop.

P-149

Successful prophylactic treatment of chronic tension-type headache with ±-2 receptor agonist, Tizanidine

*Abbas Ghorbani * (Isfahan), Bahador Asadi (Isfahan), Fariborz Khorvash (Isfahan), Majeed Ghasemi (Isfahan)*

Background: Chronic tension-type headache both is prevalent and has an impact on quality of life. It is one of the primary headache most difficult to treat. Although there is some controversy,

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Tizanidine an alpha 2-adrenergic agonist is an effective agent in the preventative treatment of Chronic tension-type headache. *Methods:* 100 patients with chronic tension-type headache were included in a randomized, double-blind, placebo-controlled, crossover trial. None of the patients had migraine, depression, opium addiction or analgesic overuse. Tizanidine 8 to 12 mg/day or placebo was each given for 12 weeks. Follow-up visits were performed at 2-week intervals *Results:* 89 patients completed the study. The calculated average of headache duration _ headache intensity, was lower during treatment with tizanidine (739.12) than during treatment with placebo (1324.63) (p = 0.01). headache frequency (p = 0.01), headache duration (p = 0.01), and headache intensity (p = 0.05) was also lower in tizanidine group and than placebo. 5 patients did not tolerate tizanidine. *Conclusions:* Tizanidine reduced average of headache duration _ headache intensity by 44.2% more than placebo in chronic tension-type headache patients. Our findings stress the efficacy of tizanidine in prophylactic treatment of tension-type headache, with remarkable improvements and few side effects.

P-150

Magnetic stimulation for migraine: autonomic nervous system effects

M Kamath (Hamilton), B Clarke (Hamilton), A Upton (Hamilton), C Castellanos (Hamilton)*

Background: This study assessed the effects of changes in cortical excitability and trigeminal pathways due to Transcranial Magnetic Stimulation (TMS) on pain and Autonomic Nervous System (ANS) balance determined by heart rate variability (HRV) measures in migraine. *Methods:* Thirty-three persons with migraine headache (29 females; mean age 43.27 plus-minus 10.81 S.D. yrs old; headache duration 8.84 plus-minus 14.65 hours) were monitored for (HRV) 5 minutes prior to and 20 minutes after application of 2 brief TMS pulses to the scalp. The HRV signal was computed from the ECG and subjected to power spectral analyses. Areas under the Low Frequency (LF) and High Frequency (HF) components of the HRV were determined and a ratio of the powers (LF:HF area) was obtained. Pain intensity was assessed on a 5 point Likert-type scale (1= best score). *Results:* Pain intensity changed from mean 3.28 plus-minus 0.82 S.D. to 2.19 plus-minus 1.09 (p less than 0.05). Mean heart rate decreased from 79.05 plus-minus 10.27 to 72.89 plus-minus 11.35 beats/min. The LF area increased from 6522 plus-minus 1277 to 8315 plus-minus 1009 (beats/min)2 (p less than 0.001). The HF area measured from 5600 plus-minus 1568 to 8755 plus-minus 3071 (beats/min) 2 (p less than 0.001). The LF:HF ratio decreased from 1.31 plus-minus 0.51 to 1.13 plus-minus 0.48 (NS). *Conclusion:* TMS produces a reduction in pain and perturbs sympathetic and parasympathetic components of the ANS.

P-151

Hydrocephalus and ophthalmoplegia: a syndrome of young adults with Whipple's disease of the tectal plate.

R Leblanc (Montreal), M-C Guiot (Montreal), D Melanson (Montreal), M Gans (Montreal), D Diorio (Montreal), A Genge (Montreal), P Rene (Montreal), R Lalonde (Montreal)*

Introduction: The clinical spectrum of cerebral Whipple's disease has yet to be fully elucidated. We describe two cases of primary Whipple's disease of the tectal plate producing stereotypical clinical and radiological manifestations. *Case Reports:* Two men aged 23 and 29 years developed headache and diplopia without systemic complaints or illnesses. Examination revealed ophthalmoplegia and papilledema. Magnetic resonance imaging demonstrated a single, enhancing lesion of the tectal plate and hydrocephalus from obstruction of the aqueduct of Sylvius. Histological examination of biopsy specimens revealed PAS-positive inclusions within macrophages and, in one case, Gram-positive rods compatible with Whipple's disease. Polymerase chain reaction and duodenal biopsy were negative in both cases. The hydrocephalus was successfully treated by CSF diversion, and both patients were treated with prolonged antibiotic therapy. *Conclusions:* Whipple's disease can affect the brain in the absence of systemic involvement, as was the case in our two patients. The diagnosis is difficult and is best achieved by biopsy. The presence of PAS-positive intracellular inclusions is highly suggestive of the disease. Ophthalmoplegia and hydrocephalus produced by an enhancing lesion of the tectal plate should suggest that T. whippelii is the causative agent. Prolonged antibiotic therapy is indicated once the diagnosis has been confirmed histologically.

P-152

Masticatory exophthalmos in a patient with hereditary neurocutaneous angiomatosis

*R Leblanc** (Montreal)*

Background: We describe the case of a patient with vascular hamartomas affecting the skin, face and brain, and exophthalmos upon mastication. *Case Report:* A 13 year-old girl was ascertained as part of a family in which males exhibited the coexistence of vascular naevi and cerebral vascular malformations. She had a painful cavernous angioma of the forearm. Magnetic resonance (MR)angiographic and ophthalmologic examinations were normal. She consulted again 5 years later because of exophthalmos occurring when she clenched her teeth or upon mastication, which in retrospect, had been present since childhood. A focal area of vascular distention was seen in the right peri-orbital region when she clenched her teeth. MR imaging demonstrated a large vascular malformation involving the right masseter extending into the lateral and retro-orbital regions, a vascular malformation of the right parotid gland, and two arteriovenous malformations of the brain. *Discussion:* Hereditary neurocutaneous angiomatosis is a recently described phacomatosis (J Neurosurg 85:1135-1142, 1996) characterized by the coexistence of vascular naevi and cerebral vascular malformations. This condition is not limited to men, as previously thought; and lesions can also involve deep facial structures and the orbit to produce exophthalmos with mastication from mechanical pressure on the globe or by venous engorgement.

P-153

What we did (not) learn in neuroanatomy: A re-test of knowledge in graduating medical students and a critical look at basic neuroscience education in the medical curriculum.

F Mateen (Saskatoon), M D'Eon (Saskatoon), R Devon (Saskatoon), R Doucette (Saskatoon)*

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Canadian medical schools vary in the method and duration of teaching neuroanatomy to students, most of whom will not specialize in the neurological sciences. Very little research exists on basic neuroscience education in the undergraduate medical curriculum. Even less is known about the retention of basic neuroscience knowledge after the initial examination of taught material. The University of Saskatchewan teaches a one-semester class dedicated to neuroanatomy. *Methods:* In November 2004, medical students of the class of 2005 at the UofS were asked to answer 20 multiple choice questions from the original midterm, given in first-year neuroanatomy (February 2002). *Results:* 31 students, doing on-site rotations, were asked to participate. 20 students responded. A majority of students received grades above 75% on the original midterm. The mean score on the retest was 6.7/20. Two students received passing grades on the retest while the other 18 did not. The range of scores was from 2/20 to 11/20. *Conclusions:* Knowledge loss was severe, less than three years after initial presentation of basic neuroanatomy material. A lack of reinforcement of taught material and irrelevance to the clinical setting may be to blame. Administration of the same questions to practicing neuroscience physicians is ongoing.

P-154

Superficial siderosis of the CNS

F Mateen (Saskatoon), C Voll (Saskatoon)*

Background: Superficial siderosis of the central nervous system is a rare and insidiously progressive cause of neurodegeneration. A source is found in only 60% of cases and is often diagnosed by T2-weighted magnetic resonance imaging (MRI). A wide variety of clinical presentations have been reported in the approximately 100 cases in the literature to date. *Methods:* A case report is presented. *Results:* A 54-year-old woman presented with a progressive lower motor syndrome, and a 9-year history of low back pain, intermittently radiating down the left leg. She took coumadin for protein C deficiency. MRI of the spine, CT myelography, electromyography, and NCS were normal. Over the next five years, she developed symptoms of urinary retention and progressive left leg weakness. NCS revealed a polyradiculopathy. Spinal and four vessel cerebral angiography were unremarkable. Repeat MRI showed extensive siderosis encompassing the cord, cerebral hemispheres, and the cauda equina. An arteriovenous malformation at the L4-L5 level was confirmed as the source of active bleeding. *Conclusion:* Diagnosis of superficial siderosis of the CNS is often diagnosed by MRI before clinical symptoms occur. This case illustrates the rare event of normal imaging studies in the presence of an AVM malformation with symptomatic progression likely exacerbated by chronic anticoagulation.

P-155

Reversible posterior encephalopathy due to severe hypercalcemia : a case report and review of the literature

F Moreau (Sherbrooke), Z Nasreddine (Longueuil), J-F Clement (Longueuil)*

Background: Reversible posterior encephalopathy syndrome includes headache, nausea, cortical visual loss, stupor and characteristic changes in the posterior regions of the brain on neuroimaging. Hypercalcemia has been described as a possible etiological factor. *Methods:* We report a case of reversible posterior encephalopathy occurring in the context of severe hypercalcemia. We reviewed the patient's relevant data and reviewed the literature from a multiple keywords MEDLINE query. *Results:* A 67 year old female presented with headache, vomiting and rapidly progressive stupor and coma. Blood pressure rose transiently to 200 mmHg systolic but the patient remained comatose while normotensive for 6 days. Investigation revealed an ionised calcium level of 1.97 and hyperintense signal on T2 and FLAIR sequences on both temporo-occipital regions crossing the posterior cerebral artery territory and sparing both calcarine sulci. Shortly after correction of the calcium level the patient recovered and MRI changes normalized. Magnetic Resonance Angiography (MRA) was normal. Of four cases reported in the literature, three had seizures. No seizures occurred in this case. *Conclusions:* Hypercalcemia is the most probable cause for the patient's encephalopathy and changes on MRI. Normal MRA further supports the microvascular hypothesis and/or direct neurotoxic effect of hypercalcemia.

P-156

Accident with a moose - an unusual cause of Vernet s syndrome

M Mouradian (Edmonton), Z Siddiqi (Edmonton)*

Introduction: Vernet's syndrome (VS) is characterized by involvement of multiple cranial nerves (IX, X, XI) in the jugular foramen. *Case Report:* While driving at night, a 63 year old man had a head-on collision with a moose, which struck the windshield and, subsequently, his face. He developed hoarse voice and dysphagia within few hours of the accident. Examination revealed a whispery-breathy voice, with uvular deviation to the right, and a drooped palate, absent gag reflex, weak (MRC scale grade 3) sternocleidomastoid and trapezius muscles and limited arm abduction with winging of medial scapular border on the right. *Results:* A CT scan revealed a basal skull fracture involving the right petrous bone and extending up to the clivus. He developed aspiration pneumonia and was found to have moose hair in his vomitus. Subsequent swallowing evaluation was markedly abnormal requiring gastric PEG placement. At six months follow up his neurological deficits remain unchanged with noticeable atrophy of the sternocleidomastoid and trapezius muscles. *Discussion:* Neurological deficits in our patient indicate involvement of the glossopharyngeal, vagus, and accessory nerves, likely due to the basal skull fracture. Though VS may be caused by a number of conditions, our patient illustrates a unique presentation of this rare condition.

P-157

The association of Papillo-Renal Syndrome, Benign intracranial hypertension and A-hypervitaminosis.

J Prévost (Sherbrooke), M-È Arsenault (Sherbrooke), F Evoy (Sherbrooke)*

Objective: To report cases of two siblings presenting papillo-renal syndrome and pseudotumor cerebri. *Background:* Papillo-renal syndrome or renal coloboma syndrome, an autosomal dominant disorder associated with mutations in PAX2, is characterized by colobomatous eye defects, renal hypoplasia, vesicouretal reflux,

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high-frequency hearing loss, and rarely central nervous system abnormalities. The association of this syndrome with benign intracranial hypertension presentation was not describe to our knowledge. *Design:* Observational cases *Results:* An older sister and her brother presented benign intracranial hypertension at the age of 15. A severe renal dysfunction was discovered for the girl, during a blood-work-up. They both have hypervitaminosis-A, obesity and chronic headache. On ophthalmic examination, the two siblings had bilateral optic disk dysplasia. Both parents are asymptomatic with normal fundoscopic exam. The PAX2 mutation research is in process. *Conclusion:* The association of benign intracranial hypertension with renal-coloboma syndrome is not clear. In our cases, we suspect that a defective vitamin A metabolism may have played an important role.

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Withdrawn

P-159

Abolition of migraine by transcranial magnetic stimulation

A Upton (Hamilton), A McComas (Hamilton)*

Background: Since there is both clinical and neurophysiological evidence for cortical hyperexcitability in migraine, transcranial magnetic stimulation (TMS) might modify attacks. A severely affected, but well studied, patient was chosen as a prototypic case for a larger study. *Methods:* The patient is a 71 year old woman with a 50 year history of familial migraine, initially basilar but later with quadriplegia, widespread body pain, and loss of consciousness. During a 6-month control period, she continued to receive anti-migraine drugs only. For the following 6-month treatment period, TMS was, whenever feasible, applied instead, using a Magstim 200 machine. The study had ethical approval. *Results:* During the treatment period, TMS abolished migraine symptoms on all 47 occasions. The action was immediate and dramatic, the effective stimulus site conforming roughly to the primary somatosensory cortical map. In addition, the frequency of attacks was reduced by over 70 percent ($p<0.001$). *Conclusions:* TMS may be of benefit even in severe, complex migraine resistant to medication. The pain-generating system appears to be located in the primary somatosensory cortex, and it is possible that TMS acts by blocking reverberating neuronal activity.

P-160

Transcranial magnetic stimulation (TMS) for migraine: clinical effect

A Upton (Hamilton), B Clarke (Hamilton),*
C Castellanos (Hamilton)

Background: The application of Transcranial Magnetic Stimulation (TMS) in various neurological disorders has been investigated. The impact on pain in migraine has not. *Methods:* of 42 patients receiving TMS (mean age 41.43 plus-minus 11.69 S.D. yrs; 36 females) 3 had an aura and pain and 2 an aura only. Two brief pulses were applied to the scalp. In total, 76 stimulations were done as part of a controlled blinded study. Pain was measured using a 5 point Likert-type scale (1=best score). Patients were allowed to take medication after treatment if necessary. *Results:* There was a mean decrease in pain of 70 percent, and in those subjects with an aura, control was 100 percent. The mean time to show improvement was 15.46 plus-minus 6.82 S.D. minutes. Of the 76 stimulations applied 32 percent reported no further recurrence of headache the next day, 24 percent had a mild, 11 percent a moderate and 33 percent severe recurrence. *Conclusions:* Preliminary results indicate that TMS is an important adjunct treatment for migraine.

P-161

Aluminum encephalopathy due to intravenous injection of boiled methadone: case report

R Yong (Vancouver), D Holmes (Vancouver),*
G Sreenivasan (Vancouver)

Background: Aluminum toxicity came to attention in the medical literature as a sequela of hemodialysis, where accumulation of aluminum in body tissues occurred secondary to the use of aluminum-containing dialysate and phosphate binders. Chronic aluminum encephalopathy is characterized by dementia, dysarthria, tremor, myoclonus, ataxia, and apraxia of speech. *Case History:* A 42-year-old man presented to medical attention for evaluation of seizures. He subsequently developed dysarthria, a hesitant pattern of speech, ataxia, myoclonic jerks, and a postural tremor. He admitted to the practice of boiling his oral methadone preparation in an aluminum pot for the purpose of redissolving the residue for intravenous injection. *Findings:* The patient's serum aluminum level was 6650 nmol/L, seventeen times the upper limit of the reference range for our laboratory. Serial electroencephalography demonstrated periodic sharp waves in couplets at a frequency of 2 Hz on a slowed and poorly organized background. The patient was treated with desferrioxamine chelation therapy, with a reduction in the serum aluminum level to 2390 nmol/L. *Conclusion:* The diagnostic work-up of intravenous drug users exhibiting multiorgan dysfunction warrants a thorough inquiry into injection drug practices. Desferrioxamine chelation therapy should be considered for the treatment of chronic aluminum toxicity in non-hemodialysis patients.

P-162

Delayed debridement in 125 civilian craniocerebral gunshot wounds

W Liebenberg (Haywards Heath), A Demetriades (Oxford),*
C Hardwidge (Haywards Heath), B Hartzenberg (Tygerberg)

Background: We practise delayed definitive debridement. Early surgery reserved for significant, acute haematomas. Basic wound care performed all cases in emergency room. *Methods:* January 1997 to October 2003. Case notes retrospectively. Outcome was based on the Glasgow Outcome Score. *Results:* Mean age 24.9 (std 10.9), 111(88.8%) were male. 15 suicide cases 4 tangential GSW. Mean presenting GCS 7.33. In 70.4% presenting GCS 3-8, in 7.2% GCS 9-12 and 22.4% GCS 13-15. Forty nine cranial procedures performed 27 patients: delayed debridement (21/26), emergency surgery (4/26), delayed external ventricular drainage (1/26). Average time to delayed definitive debridement 12.2 days. Infection 8 patients (15.7% of survivors) 3 meningitis, 4 brain abscesses one

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meningitis and brain abscess. Total mortality 69.6% (87/125). Discharge Glasgow Outcome Score (GOS) poor (GOS 1-3) in 89 (71.2%) (only 2 with GOS 2 or 3) and good (GOS 4 or 5) in 36 (28.8%). Predictors poor outcome: low presenting GCS, intubation in the field and transventricular tract on CT. *Conclusions:* We report on a protocol of delayed debridement secondary to wound care and closure as primary procedure. Within the setting of limited resources the results suggest this would be an acceptable management strategy for penetrating craniocerebral GSW.

P-163

Sedative medication may selectively affect the vestibular-ocular reflex.

S Morrow (London), GB Young (London)*

Introduction: Vestibulo-ocular reflex (VOR) testing is an essential component of the clinical assessment of brainstem function. VOR is tested using the oculocephalic reflex (OCP) and the oculovestibular reflex (OVR), or cold calorics. Loss of the VOR often prompts consideration of structural brainstem damage or Wernicke's encephalopathy. *Methods:* We report 3 comatose patients with absent VOR as an isolated finding on initial neurological assessment. *Results:* Three male patients, aged 45-74 years, each received midazolam prior to the initial examination. One also received propofol, while another received lorazepam and fentanyl. Two presented with intentional drug overdoses, while the third patient had a complicated course post-cardiac surgery. All three patients initially had absent responses to OCR and cold calorics bilaterally, but all other brainstem functions were normal. Each patient regained both OCR and OVR within 1 day after sedative medication had been removed and ultimately recovered completely. Neuro-imaging and screening for Wernicke's encephalopathy were negative. *Conclusions:* Sedatives, especially benzodiazepines, may transiently and selectively abolish the VOR; this is helpful in the evaluation of the comatose patient.

General Neurosurgery

P-164

Preventing brain and spinal cord injuries in primary school children: an assessment of injury-related behavioural intentions using healthscope

J Atkinson (Toronto), M Cusimano (Toronto), B Azizi (Toronto), I Kalnins (Toronto), M Chipman (Toronto), T Bekele (Toronto)*

Background: The Think First for Kids (TFFK) safety curriculum is being evaluated in a randomized controlled trial. It is important to understand children's intentions to engage in safe and unsafe behaviours and the reasons that underlie their choice. *Methods:* A scenario-based questionnaire, HealthScope, was developed to examine children's safety-related behavioural intentions. Children were presented with vignettes where they must choose between engaging in a safe or unsafe action and provide a reason for their choice. Reasons were constructed based on the following influences, friends, parents, personal habits, safety concerns and the law. *Results:* Analyses from 2800 children in the intervention and the control group show that across all vignettes children intend to choose the safe course of action more than 80% of the time. Males are less likely to choose the safe response. Safe decisions were mostly driven by concern for safety (45%), while influences of parents (5.9%) and friends (5.5%) were the least important factors. Unsafe decisions were mostly driven by habit (43%). There was no significant difference between pre/post tests and groups. *Conclusions:* Behavioural intentions provide insights into how children might apply knowledge gained from TFFK. Results will aid in the design of injury prevention programs for children.

P-165

Superficial femoral vein invasion by a benign neurofibroma

C Chatillon (Montreal), M Guiot (Montreal), M Corriveau (Montreal), L Jacques (Montreal)*

Background: Neurofibromas are benign neural sheath tumours arising from intraneural supporting cells. This report aims to document a rare occurrence of vascular invasion by a benign neurofibroma, i.e. without microscopic evidence of malignant transformation. *Methods:* Mrs W. is a 40 year-old woman who presented to clinic with a 4 year history of right thigh mass associated with diffuse lower extremity pain. She had intact motor function and dysesthesia in the femoral distribution. She had no other clinical manifestations of neurofibromatosis. MRI revealed an ill-defined 1.8 x 2.1 x 4 cm enhancing mass in the anteromedial aspect of the right thigh closely associated with the superficial femoral vein. Upon exposure for resection, the mass was infiltrating a segment of the superficial femoral vein. The vessel segment and mass were therefore resected "en bloc" after proximal and distal ligation of the vein. *Results:* Pathological examination of the specimen confirmed the diagnosis of neurofibroma without any evidence of sarcomatous changes, and involvement of the vessel wall with thrombosis and recanalization. *Conclusion:* This case brings to light unusually invasive behavior by this benign tumour type. Such occurrence is rare and has not been reported previously in the literature to our knowledge.

P-166

Using geomatics to understand and prevent traumatic brain injury

M Cusimano (Toronto), K Jones (Toronto), M Chipman (Toronto), I Johnson (Toronto), R Glazier (Toronto), V Grant (Toronto), K Arena (Toronto), P Bermingham (Toronto), T Bekele (Toronto), J Atkinson (Toronto)*

Background: Understanding the demographics of Traumatic Brain Injury (TBI) is important for TBI prevention and control. *Methods:* The demographics of residence location of 165 patients with severe brain injuries (AIS greater than 3) and alcohol levels of greater than 12mmol/l were compared to those of the overall referral area of an urban neurosurgical unit. Indices based on a ratio of census variables in the residence location 6-digit postal codes compared to the average for the referral area were developed for all 2001 Canadian Census variables. Cluster analyses of these indexes were used to identify determinants with common variance that

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explained the geographic patterns of the occurrence of alcohol associated TBI. *Results:* One cluster buffered at 100 meters captured 81% of cases and 62% of the referral area. This cluster consisted of areas with Lower Income, Government Compensation, Multi Family Households, Persons employed in the manufacturing trades, and a lack of people employed in the managerial occupations. Two clusters identified 85% of cases. *Conclusions:* TBI with alcohol occurs in persons who reside in areas with higher rates of Lower Income, Government Compensation, low unemployment, Multi Family Households, persons employed in the manufacturing trades and lower rates of persons employed in managerial occupations.

P-167

Injury prevention curriculum improves student injury-related behaviours: feedback from teachers implementing Think First for Kids

M Cusimano (Toronto), J Atkinson (Toronto), K Li (Toronto), I Kalnins (Toronto), M Chipman (Toronto), B Freedman (Toronto), T Bekele (Toronto)*

Background: We are conducting an evaluation of the Think First for Kids (TFFK) injury prevention program. The study involves 987 teachers from 23 school boards across Ontario. Our objective is to document the immediate benefits and limitations of the TFFK curriculum, particularly as viewed by teachers regarding student injury-related behaviours. *Methods:* Teachers provided details into the administration of the curriculum and evaluation processes related to injury prevention. The amount of time spent teaching injury prevention, the number of injuries observed, and changes in students' daily safety behaviour were documented by the teachers through questionnaires. *Results:* In 2002, 442 questionnaires were returned (42 percent response rate) and in 2003, 341 questionnaires were returned (35 percent response rate). Changes in student behaviour were observed most frequently after the first year of program implementation (p-value less than .005) and these changes persisted in subsequent years but did not increase. Twenty percent of students demonstrated behavioural changes with no education in injury prevention; in contrast 66 percent of students demonstrated behavioural changes after one year of TFFK (p-value less than .005). *Conclusions:* Education is effective in changing observed injury-related behaviour of students, and continuous reinforcement may prevent a decay of this knowledge.

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Knowledge translation in communities: community readiness for injury prevention programming

M Cusimano (Toronto), J Dang (Toronto), M Chipman (Toronto), I Kalnins (Toronto), B Freedman (Toronto), J Atkinson (Toronto), T Bekele (Toronto)*

Background: Assessing a community's readiness for injury prevention programs is important because such programs can only be successful when the target audience is ready to accept information. Readiness of communities was assessed using Community Readiness Model (CmRM) and the Coalition Readiness Model (ClRM) as part of the Think First for Kids Injury Prevention program (TFFK). *Methods:* Surveys were sent to principals and school council chairs. A total of 138, 64 from program schools (PS) implementing TFFK program and 74 from pre-program (pPS) schools using regular health and safety curriculums prior to starting TFFK, were returned. Schools' level of readiness, measured by mean scores of CmRM and ClRM, were compared between these two groups. *Results:* Using the CmRM, the level of readiness between PS (Mean: 4.2 Std.Dev: 1.7) and pPS (Mean: 4.6 Std.Dev:1.6) were different. However, this difference was not statistically significant (p-value: 0.3). ClRM measures found no difference in readiness between PS and pPS. The largest portion of schools (30 percent) was in the preplanning stage. *Conclusion:* There were no significant differences between the two groups in a TFFK randomized controlled study. The CmRM and the ClRM were effective means of assessing readiness of communities to implement prevention programs.

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Academic Productivity of Canadian Neurosurgeons

B Jhawar (Windsor), M Cusimano (Toronto)*

Introduction: The objective of this project was to determine the academic productivity of Canadian neurosurgeons. *Methods:* Using Visual Basic, Perl and Endnote we developed algorithms to search the affiliation category of the National Library of Medicine. We extracted all publications where the first authors identified his/her affiliation with a department of neurosurgery (1988-2003). To validate this method we manually reviewed the affiliation category of all articles published on page 1 of all journals in 2003 (n=5852); 31.3% had no author affiliation; the sensitivity was 93.1% and the specificity was 100%. *Results:* The number of publications by Canadian departments of neurosurgery doubled between 1988 (n=69) and 2003 (n=138), but as a fraction of all neurosurgical articles there was little change (3.5% to 3.6%). Canadians were most productive in 1999 (4.4%). Although the United States and Japan produced the majority of publications, both nations demonstrated a decline in productivity over recent years. When we divided the number of publications produced in 2003 by the number of neurosurgeons in each province, the number of articles produced per neurosurgeon were; Quebec=16.0; Ontario=7.2; Manitoba=3.0; Alberta=2.9; Saskatchewan=2.6; BC=1.9; Nova Scotia=1.4; and Newfoundland=1.3. *Conclusion:* Canadian neurosurgeons have been academically productive despite their limited numbers. Productivity by province varies and possible reasons are discussed.

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Cancelled

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Reversal of a secondary Chiari malformation using a programmable lumboperitoneal shunt in the treatment of recalcitrant idiopathic intracranial hypertension

F Lam (Edmonton), V Mehta (Edmonton)*

Background: Treatment of idiopathic intracranial hypertension (IIH) with lumbar CSF diversion may cause a secondary Chiari malformation. We present a complex case of symptomatic secondary Chiari malformation in a 20 year-old female following exhaustive medical and surgical therapy. The objective of this report is to

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illustrate how switching from a valved LP shunt to a programmable valve dealt with these complex cerebrospinal dynamics. *Methods:* Retrospective chart review of a 20 year-old female presented to our clinic followed over a 3 year period. *Results:* This patient initially presented as an adolescent with IIH. She was medically managed following her diagnosis, but eventually underwent an optic nerve sheath fenestration for acute vision changes. Exacerbation of her symptoms 5 years later led to the insertion of a low-pressure LP shunt and subsequent development of a secondary Chiari malformation. She continued to present with persistent occipital headaches, facial numbness in the background of a functioning LP shunt. Shunt replacement with a Codman-Medos valve in an attempt to control her fluctuating symptoms. She presented 2 months later following repeated valve adjustments with reversal of her Chiari malformation and no evidence of a syrinx. *Conclusion:* Utilization of a programmable LP shunt may be beneficial in complex cases of IIH

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Reading emergency CT scans and acting on them: how much confusion is there amongst referring physicians?

W Liebenberg (Haywards Heath), A O'Brien (Haywards Heath), M Tait (Haywards Heath), J Norris (Haywards Heath)*

Background: CT scan interpretation is a basic, important skill determining referral patterns to neurosurgery. We postulated that this is an under developed skill. *Methods:* We designed a questionnaire with 12 CT's, gathered information about the doctor filling in the form, whether the CT's were abnormal, suspected pathology (picklist), confidence of the answer and whether emergency referral indicated (focal signs or absence of neurological deficit). *Results:* 74 questionnaires, 67 doctors were in training, 52 first 5 years following qualification. Six planned careers in neurosciences, radiology. 77.7% scans correctly identified abnormal or not. Correct diagnosis 39.7%. In 61.9% the respondents were confident of diagnosis. Subarachnoid haemorrhage (SAH) diagnosed 24.3%, acute subdural haemorrhage (ASDH) 37.8%, acute extradural haemorrhage (AEDH) 41.9%, isodensed chronic subdural haematoma 21.6% base of skull fracture 75.7%. In 62%, patient with SAH absence focal signs would not have been referred acutely. In 58% and 59% respectively (in the absence of focal signs) ASDH and AEDH would be referred acutely. *Conclusions:* The correct interpretation of CT scans is poor at the emergency room level. Most patients, even in the absence of focal signs would be referred acutely despite confusion about the diagnosis. Work must be done to improve on this.

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Suicidal gunshot wounds to the head: Symptom of a privileged society?

W Liebenberg (Haywards Heath), A Demetriades (Oxford), B Hartzenberg (Tygerberg)*

Background: We postulated that attempted suicides by gunshot wounds of the brain occurred mostly in the privileged part of the society and that homicide related shootings would be restricted to the poorer and mostly non white suburbs. *Methods:* Retrospectively reviewed all attempted suicides from our database of craniocerebral gunshot wounds from Jan 1996 to October 2003. Of 194, 125 had dural penetration and 15/125 attempted suicides. *Results:* Average age 28.13 (11-56) male preponderance 86.7% and 60% white. Only 2 attempted suicides during winter months. Presenting GCS 8/15 or lower in 13. Seven presented fixed and dilated pupils. Only 4/15 survived, all Glasgow Outcome Score 4 and 5. Mortality was 73.3% compared to 69% of the remaining 110 homicide related patients. Average length hospital stay survivors 24.25 days (8-46) average 4.6 days (1-10) in ICU. Of 125 with dural penetration, only 12 white of which only 3 homicide victims. *Conclusions:* Homicide related penetrating gunshot wound of the brain nearly exclusively symptom of non white residents. White males more prone to attempted suicides. Average age disturbingly low. Suicide related cases have a high mortality but not significantly more than the rest of the study population.

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The contributions of Penfield's neuropathological studies to his surgical technique

K Mukhida (Toronto) , W Feindel (Montreal)*

Previous reports have described Wilder Penfield's clinical training with William Halsted, Harvey Cushing, and Otfrid Foerster as forming the technical basis of his surgical techniques. Less has been explored of the contributions that Penfield's neuropathological studies made to his neurosurgical practice. Penfield admitted that mastery of neurophysiology, neuroanatomy, and neuropathology was prerequisite to earning a living as a neurosurgeon and consequently undertook anatomical studies in Spain with Santiago Ramón y Cajal and his student Pio del Rio Hortega in 1924. Penfield's time in Madrid investigating nervous system histology using the Spaniards' silver stains was productive and motivating and gave him the basis for a scientific approach to his neurosurgical treatments for epilepsy and brain tumours. Using Penfield's publications based on his Spanish experiments as well as his correspondences regarding his time in Spain, this paper evaluates the role Penfield's neuropathological experiences in Spain had on his neurosurgical operative techniques. Specifically, how did Penfield's studies of glia affect his approaches for the resection of glial tumours? How did his basic science appreciation of scar formation affect the formulation of his techniques of cortical resection for the treatment of medically refractory focal epilepsy and complement his electrophysiological studies of cortical localization?

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International neurosurgical education: a Nepalese experience

K Mukhida (Toronto), S Shilpakar (Kathmandu), M Sharma (Kathmandu), M Bagan (Kathmandu)*

Although the concept of the global village portrays populations as forming interdependent communities with similar health needs (Taylor, Can J Surg 1999), there are inequities in the provision of neurosurgical services throughout the world. One of the ways to improve neurosurgical care in the developing world is through international medical education. This strategy was recently applied at the Tribhuvan University Teaching Hospital (TUTH) in Kathmandu when an American neurosurgeon moved to Nepal in

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1995 to train Nepalese surgeons locally. The growth of the neurosurgical department at TUTH validates the ability of international neurosurgical education programs to support the development of neurosurgery programs in the developing world without detrimentally affecting other health care areas. This paper traces the origins of neurosurgery in Nepal, outlines the specialty's development in Kathmandu at TUTH over the past decade from international education strategies, and describes the current status of and challenges facing the provision of neurosurgical care in Nepal. The role of neurosurgical services in improving the health care status of populations in developing countries is considered. Neurosurgeons in developing and developed countries alike should continue to work to remedy the inequitable distribution of neurosurgical knowledge and services throughout the world.

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Calvarial remodeling and duraplasty as a treatment for progressive diaphyseal dysplasia (Camurati-Engelmann disease).

Richard Reid (Halifax), Charles Maxner (Halifax), William Howes (Halifax)*

Background: Camurati-Engelmann disease (CED) or progressive diaphyseal dysplasia is a rare, sclerosing dysplasia inherited in an autosomal dominant manner. Recently the gene causing CED has been found on chromosome 19q13. This region contains the gene encoding an important mediator in bone remodeling called Transforming Growth Factor Beta 1 (TGFB1). Patients present with variable osseous and muscular manifestations. The femurs are most commonly affected however osteosclerotic dysplasia of the skull occurs in over half of the patients. *Methods:* We present a case of a 38-year old man who presented with a long history of headaches and progressive visual loss secondary to papilloedema. After exhausting all conventional medical and surgical treatment options the calvarial remodeling and duraplasty surgery was used for treatment. *Results:* The patient had his calvarial remodeling and duraplasty surgery in May 2004 and tolerated the procedure quite well. Postoperatively he experienced resolution of his visual symptoms and disappearance of his papilloedema. *Conclusions:* CED is a rare genetic disorder that may present with progressive visual impairment from raised intracranial pressure secondary to cranial vault thickening. If the neurological compromise is not improved with standard medical or surgical procedures then calvarial remodeling and duraplasty is an option for treatment.

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Frameless stereotactic biopsy with enhanced vascular and cortical reconstructions: a review of 83 cases

*R Schapiro** (Montreal), R Leblanc (Montreal), A Olivier (Montreal), L Soualmi (Montreal), R DelMaestro (Montreal), D Sirhan (Montreal), L Jacques (Montreal), B Goulet (Montreal), A Sadikot (Montreal)*

Background: The role of frameless stereotactic biopsy (FSB) is still being elucidated as the technology for its performance evolves. We report (83) consecutive cases of FSB using novel software for enhanced vascular and cortical reconstruction. *Methods:* Fifty-one men and 32 woman aged 18 to 79 years underwent global MRI- or CT-based (2 cases) FSB for 37 superficial and 26 deep lesions. Registration was achieved using anatomical reference points; and the entry point, target, and trajectory were planned after enhanced vascular and cortical reconstruction to avoid eloquent cortex and all major vessels along the path of the biopsy needle. Biopsy results and complications are reported. *Results:* The 83 patients underwent one to 11 biopsies (total: 267 passes). A histological diagnosis was achieved at the initial operation in 80 patients and in three others after a second surgery: there were 53 gliomas of various grades, 6 lymphomas, 4 metastases, and various other lesions. There was one complication, a biopsy-related intra-tumoral haematoma requiring evacuation. *Conclusions:* Histological diagnosis of mass lesions can be achieved in the majority of cases using FSB. Enhanced vascular and cortical image-reconstruction may minimize the risk of neurological complications by identifying a trajectory that avoids eloquent cortex and major vessels.

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Delayed neuronal death after attempted hanging

S Siddiqi (London), S Krawitz (London), B Young (London)*

Background: In suicidal hanging death is usually due to asphyxiation or occipital-cervical dissociation followed by cardiac arrest. We describe a unique case of delayed neuronal death. *Case History:* A 32 year old, Type 1 diabetic male hung himself for less than five minutes before rescue. Cardiac arrest did not occur but the pulse was weak. He breathed and exhibited decerebrate posturing. Initial CT scan was unremarkable. He was in diabetic ketoacidosis; anion gap and serum glucose were corrected by day 2, when an EEG without sedation showed low voltage delta activity with spontaneous variability and minimal reactivity. On day 3 he opened his eyes and obeyed simple commands. EEG showed reactivity and mild suppression. By day 4 he became comatose without apparent cause. EEG showed suppression, intermittent rhythmic delta and no reactivity. MRI showed diffuse neocortical and putaminal ischemic changes. He died two days later. Autopsy showed ischemic neuronal change in the putamina and large cell layers of the neocortex; thalamus and cerebellum were spared and large vessels were patent. *Conclusion:* Delayed deterioration after hanging related to the development or exacerbation of cerebral cortical damage. Possible mechanisms will be discussed. This has prognostic and therapeutic implications.

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Automated Fusion Technique for Fusion of MRI and CT for Visualization of Subdural Electrodes

D Steven (London), A Parrent (London), S Wiebe (Calgary), S Mirsattari (London)*

Background: Precise epileptic focus localization is crucial for the surgical treatment of medically intractable epilepsy. Intracranial recording with subdural electrodes is indicated when noninvasive techniques are inconclusive. Visualization of electrode contacts in relationship to the cortical surface is required to translate the electrocorticogram into a surgical plan. Methods to do this include plain skull x-rays, CT scanning, MR scanning and image fusion techniques. Each has significant drawbacks, which our method

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overcomes. *Methods:* For each patient, a pre-operative 3D SPGR MRI acquisition was registered to a post-operative CT scan using a volumetric mutual information algorithm. After registration, the skull and skin tissues are removed from the MRI and the subdural electrodes are segmented from the CT scan. *Results:* Processing time is 60-90 seconds on a 2 Ghz PC, and requires no user intervention. Volume rendered views of the brain with superimposed electrodes are displayed in an interactive fashion. *Conclusions:* The method has been applied to over 30 cases, and is being used at 3 centres across Canada. It overcomes the lack of brain visualization in plain x-rays and CT-scans, the electrode-induced artifacts in post-operative MRI, and the user/time intensive aspects of previous image fusion approaches.

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Ventriculoperitoneal shunt obstruction presenting with hemiplegia and porencephalic cyst

D Zhang (Edmonton), R Fox (Edmonton)*

Ventriculoperitoneal shunt obstruction usually presents with generalized symptoms of decreased LOC, nausea, vomiting, etc. We describe the case of a 25-year-old male presenting with a four-day history of progressive hemiplegia, decreased LOC and right-sided conjugate gaze preference. He had a history of Chiari II Malformation with hydrocephalus shunted at birth. Despite a complicated childhood course, the last shunt revision was performed 18 years ago. MR and CT imaging revealed a right frontal 2-cm superficial cystic lesion adjacent to the ventricular catheter with subtle cyst wall enhancement following gadolinium administration. Dramatic unilateral lobar edema surrounded the cyst, causing subfalcine herniation. Given the unusual clinical presentation and imaging, we elected to externalize the ventricular system and to explore the cyst to rule out infection. At surgery a simple porencephalic cyst was encountered, and following negative 48-hour cultures, a standard shunt revision was carried out. Within 24 hours, the presenting symptoms resolved. Repeat CT scan showed resolution of the lobar edema and porencephalic cyst. At 8 months postoperatively, the patient remains asymptomatic. The role of altered ventricular compliance in the formation of porencephalic cysts is addressed in the discussion.

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Mirapex®

Pramipexole dihydrochloride
0.25, 0.5, 1.0, 1.5 mg Tablets

THERAPEUTIC CLASSIFICATION

AntiParkinsonian Agent / Dopamine Agonist

INDICATIONS AND CLINICAL USE

MIRAPEX (pramipexole dihydrochloride) is indicated in the treatment of the signs and symptoms of idiopathic Parkinson's disease.
MIRAPEX may be used both as early therapy, without concomitant levodopa and as an adjunct to levodopa.

CONTRAINDICATIONS

MIRAPEX (pramipexole dihydrochloride) is contraindicated in patients who have demonstrated hypersensitivity to MIRAPEX or the excipients of the drug product (see PHARMACEUTICAL INFORMATION).

WARNINGS

Sudden Onset of Sleep: Patients receiving treatment with Mirapex (pramipexole) and other dopaminergic agents have reported suddenly falling asleep while engaged in activities of daily living, including operating a motor vehicle, which has sometimes resulted in accidents. Although some of the patients reported somnolence while on MIRAPEX, others perceived that they had no warning signs, such as excessive drowsiness, and believed that they were alert immediately prior to the event[1].
Physicians should alert patients of the reported cases of sudden onset of sleep, bearing in mind that these events are NOT limited to initiation of therapy. Patients should also be advised that sudden onset of sleep has occurred without warning signs. If drowsiness or sudden onset of sleep should occur, patients should immediately contact their physician.
Until further information is available on the management of this unpredictable and serious adverse event, patients should be warned not to drive or engage in other activities where impaired alertness could put themselves and others at risk of serious injury or death (e.g., operating machines).
Substituting other dopamine agonists may not alleviate these symptoms, as episodes of falling asleep while engaged in activities of daily living have also been reported in patients taking these products.
Presently, the precise cause of this event is unknown. It is known that many Parkinson's disease patients experience alterations in sleep architecture, which results in excessive daytime sleepiness or spontaneous dozing, and that dopaminergic agents can also induce sleepiness. There is insufficient information to determine whether this event is associated with MIRAPEX (pramipexole), all dopaminergic agents, or Parkinson's disease itself.
Hypotension: Dopamine agonists appear to impair the systemic regulation of blood pressure with resulting postural (orthostatic) hypotension specially during dose escalation. Postural (orthostatic) hypotension has been observed in patients treated with MIRAPEX (pramipexole dihydrochloride). Therefore, patients should be carefully monitored for signs and symptoms of orthostatic hypotension especially during dose escalation (see DOSAGE AND ADMINISTRATION) and should be informed of this risk (see INFORMATION FOR THE PATIENT).
In clinical trials of MIRAPEX, however, and despite clear orthostatic effects in normal volunteers, the reported incidence of clinically significant orthostatic hypotension was not greater among those assigned to MIRAPEX than among those assigned to placebo. This result is clearly unexpected in light of the previous experience with the risks of dopamine agonist therapy.
While this finding could reflect a unique property of MIRAPEX, it might also be explained by the conditions of the study and the nature of the population enrolled in the clinical trials. Patients were very carefully titrated, and patients with active cardiovascular disease or significant orthostatic hypotension at baseline were excluded.
Hallucinations: Hallucinations and confusion are known side effects of treatment with dopamine agonist and levodopa. Hallucinations were more frequent when MIRAPEX was given in combination with levodopa in patients with early disease.
Patients should be aware of the fact that hallucinations (mostly visual) can occur.
In the double-blind, placebo-controlled trials in early Parkinson's disease, hallucinations were observed in 9% (35 of 388) of patients receiving MIRAPEX, compared with 2.6% (6 of 235) of patients receiving placebo. In the double-blind, placebo-controlled trials in advanced Parkinson's disease, where patients received MIRAPEX and concomitant levodopa, hallucinations were observed in 16.5% (43 of 260) of patients receiving MIRAPEX compared with 3.8% (10 of 264) of patients receiving placebo.
Hallucinations were of sufficient severity to cause discontinuation of treatment in 3.1% of the early Parkinson's disease patients and 2.7% of the advanced Parkinson's disease patients compared with about 0.4% of placebo patients in both populations.
Age appears to increase the risk of hallucinations. In patients with early Parkinson's disease, the risk of hallucinations was 1.9 times and 6.8 times greater in MIRAPEX patients than placebo patients <65 years old, and >65 years old, respectively. In patients with advanced Parkinson's disease, the risk of hallucinations was 3.5 times and 5.2 times greater in MIRAPEX patients than placebo patients <65 years old, and >65 years old, respectively.
Neuroleptic Malignant Syndrome: A symptom complex resembling the neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, and autonomic instability), with no other obvious etiology, has been reported in association with rapid dose reduction, withdrawal of, or changes in anti-Parkinsonian therapy, including MIRAPEX.

PRECAUTIONS

Renal: Since MIRAPEX (pramipexole dihydrochloride) is eliminated through the kidneys, caution should be exercised when prescribing MIRAPEX to patients with renal insufficiency (see Pharmacokinetics and DOSAGE AND ADMINISTRATION).
Dyskinesia: MIRAPEX may potentiate the dopaminergic side effects of levodopa and may cause or exacerbate preexisting dyskinesia. Decreasing the dose of levodopa may ameliorate this side effect.
Retinal Pathology in Albino Rats: Pathologic changes (degeneration and loss of photoreceptor cells) were observed in the retina of albino rats in the 2-year carcinogenicity study with pramipexole. These findings were first observed during week 76 and were dose-dependant in animals receiving 2 mg/kg/day (25/50 male rats, 10/50 female rats) and 8 mg/kg/day (44/50 male rats, 37/50 female rats). Plasma AUCs at these doses were 2.5 and 12.5 times the AUC seen in humans at the maximal recommended dose of 4.5 mg per day. Similar findings were not present in either control rats, or in rats receiving 0.3 mg/kg/day of pramipexole (0.3 times the AUC seen in humans at the 4.5 mg per day dose).
Studies demonstrated that pramipexole at very high dose (25 mg/kg/day) reduced the rate of disk shedding from the photoreceptor rod cells of the retina in albino rats; this reduction was associated with enhanced sensitivity to the damaging effects of light. In a comparative study, degeneration and loss of photoreceptor cells occurred in albino rats after 13 weeks of treatment with 25mg/kg/day of pramipexole (54 times the highest clinical dose on a mg/m^2 basis) and constant light (100 lux) but not in Brown-Norway rats exposed to the same dose but higher light intensities (500 lux).
The albino rats seem to be more susceptible than pigmented rats to the damaging effect of pramipexole and light. While the potential significance of this effect on humans has not been established, it cannot be excluded that human albinos (or people who suffer from albinismus oculi) might have an increased susceptibility to pramipexole compared to normally pigmented people. Therefore, such patients should take MIRAPEX only under ophthalmological control.
Rhabdomyolysis: A single case of rhabdomyolysis occurred in a 49-year old male with advanced Parkinson's disease treated with MIRAPEX. The patient was hospitalized with an elevated CPK (10.631 IU/L). The symptoms resolved with discontinuation of the medication.
Use in the Elderly: MIRAPEX total oral clearance was approximately 25 to 30% lower in the elderly (aged 65 years and older) as a result of a decline in pramipexole renal clearance due to an age-related reduction in renal function. This resulted in an increase in elimination half-life from approximately 8.5 hours to 12 hours (see Pharmacokinetics).
In clinical studies, 40.8% (699 of 1715) of patients were between the ages of 65 and 75 years, and 6.5% (112 of 1715) of patients were >75 years old. There were no apparent differences in efficacy or safety between older and younger patients, except that the relative risk of hallucination associated with the use of MIRAPEX was increased in the elderly.
Pediatric Use: The safety of MIRAPEX in pediatric patients has not been established.
Carcinogenesis, Mutagenesis, Impairment of Fertility: Two-year carcinogenicity studies have been conducted with pramipexole in mice and rats. In rats, pramipexole was administered in the diet, at doses of 0.3, 2 and 8 mg/kg/day. The highest dose corresponded to 12.5 times the highest recommended clinical dose (1.5 mg t.i.d.) based on comparative AUC values. No significant increases in tumors occurred.
Testicular Leydig cell adenomas were found in male rats as follows: 13 of 50 control group A males, 9 of 60 control group B males, 17 of 50 males given 0.3 mg/kg/day, 22 of 50 males given 2 mg/kg/day, and 22 of 50 males given 8 mg/kg/day. Leydig cell hyperplasia and increased numbers of adenomas are attributed to pramipexole-induced decreases in serum prolactin levels, causing a down-regulation of Leydig cell luteinizing hormone (LH) receptors and a compensatory elevation of LH secretion by the pituitary gland. The endocrine mechanisms believed to be involved in rats are not relevant to humans.
In mice, pramipexole was administered in the diet, at doses of 0.3, 2 and 10 mg/kg/day. The highest dose corresponded to 11 times the highest recommended clinical dose on a mg/m^2 basis. No significant increases in tumors occurred.
Pramipexole was not mutagenic in a battery of *in vitro* and *in vivo* assays including the Ames assay and the *in vivo* mouse micronucleus assay.
In rat fertility studies, pramipexole at a dose of 2.5 mg/kg/day, prolonged the estrus cycle and inhibited implantation. These effects were associated with a reduction in serum levels of prolactin, a hormone necessary for implantation and maintenance of early pregnancy in rats.
Pregnancy: There are no studies of MIRAPEX in pregnant women. Because animal reproduction studies are not always predictive of human response, MIRAPEX should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus.
Pramipexole, at a dose of 2.5 mg/kg/day inhibited implantation. Pramipexole, at a dose of 1.5 mg/kg/day (4.3 times the AUC observed in humans at the maximal recommended clinical dose of 1.5 mg t.i.d.) resulted in a high incidence of total resorption of embryos. This finding is thought to be due to the prolactin lowering effect of pramipexole. Prolactin is necessary for implantation and maintenance of early pregnancy in rats, but not in rabbits and humans. Because of pregnancy disruption and early embryonic loss, the teratogenic potential of pramipexole could not be assessed adequately.
In pregnant rabbits which received doses up to 10 mg/kg/day during organogenesis (plasma AUC 71 times that seen in humans at the 1.5 mg t.i.d. dose), there was no evidence of adverse effects on embryo-fetal development. Postnatal growth was inhibited in the offspring of rats treated with a 0.5 mg/kg/day dose of pramipexole during the latter part of pregnancy and throughout lactation.
Nursing Mothers: The excretion of pramipexole into breast milk has not been studied in women. Since MIRAPEX suppresses lactation, it should not be administered to mothers who wish to breast-feed infants.
A single-dose, radio-labelled study showed that drug-related materials were excreted into the breast milk of lactating rats. Concentrations of radioactivity in milk were three to six times higher than concentrations in plasma at equivalent time points.
Laboratory Tests: There are no specific laboratory tests recommended for the management of patients receiving MIRAPEX.

Drug Interactions

AntiParkinsonian Drugs: In volunteers (N = 11), selegiline did not influence the pharmacokinetics of pramipexole.
Population pharmacokinetic analysis suggests that amantadine is unlikely to alter the oral clearance of pramipexole (N = 54). Levodopa/carbidopa did not influence the pharmacokinetics of pramipexole in volunteers (N = 10). Pramipexole did not alter the extent of absorption (AUC) or elimination of levodopa/carbidopa, although it increased levodopa C_{max} by about 40%, and decreased T_{max} from 2.5 to 0.5 hours.
Cimetidine: Cimetidine, a known inhibitor of renal tubular secretion of organic bases *via* the cationic transport system, increased MIRAPEX AUC by 50% and increased its half-life by 40% in volunteers (N = 12).
Probenecid: Probenecid, a known inhibitor of renal tubular secretion of organic acids *via* the anionic transport system, did not influence the pharmacokinetics of MIRAPEX in volunteers (N = 12).
Other Drugs Eliminated *via* Renal Secretion: Concomitant therapy with drugs secreted by the renal cationic transport system (eg, amantadine, cimetidine, ranitidine, diltiazem, triamterene, verapamil, quinidine, and quinine), will decrease the oral clearance of MIRAPEX and thus, necessitate a reduction in the dosage of MIRAPEX. In case of concomitant therapy with these kind of drugs (incl. amantadine) attention should be paid to signs of dopamine overstimulation, such as dyskinesias, agitation or hallucinations. In such cases a dose reduction is necessary. Concomitant therapy with drugs secreted by the renal anionic transport system (e.g. cephalosporins, penicillins, indomethacin, hydrochlorothiazide and chlorpropamide) are not likely to have any effect on the oral clearance of MIRAPEX.
Because of possible additive effects, caution should be advised when patients are taking other sedating medication or alcohol in combination with MIRAPEX and when taking concomitant medication that increase plasma levels of pramipexole (e.g. cimetidine).
CYP Interactions: Inhibitors of cytochrome P450 enzymes would not be expected to affect MIRAPEX elimination because MIRAPEX is not appreciably metabolized by these enzymes *in vivo* or *in vitro*. MIRAPEX does not inhibit CYP1A2, CYP2C9, CYP2C19, CYP2E1, and CYP3A4. Inhibition of CYP2D6 was observed with an apparent Ki of 30 μM, indicating that MIRAPEX will not inhibit CYP enzymes at plasma concentrations observed following the highest recommended clinical dose (1.5 mg tid).
Dopamine Antagonists: Since MIRAPEX is a dopamine agonist, dopamine antagonists such as the neuroleptics (phenothiazines, butyrophenones, thioxanthines) or metoclopramide may diminish the effectiveness of MIRAPEX and should ordinarily not be administered concurrently.

Drug/Laboratory Test Interactions

There are no known interactions between MIRAPEX and laboratory tests.

Psycho-Motor Performance

(See Warnings - Sudden Onset of Sleep).

Dependence Liability

MIRAPEX has not been systematically studied in animals or humans for its potential for abuse, tolerance, or physical dependence. However, in a rat model on cocaine self-administration, MIRAPEX had little or no effect.

ADVERSE REACTIONS

During the premarketing development of MIRAPEX (pramipexole dihydrochloride), patients enrolled in clinical trials had either early or advanced Parkinson's disease. Apart from the severity and duration of their disease, the two populations differed in their use of concomitant levodopa therapy. Namely, patients with early disease did not receive concomitant levodopa therapy during treatment with MIRAPEX, while those with advanced Parkinson's disease did.
Because these two populations may have differential risk for various adverse events, adverse event data will be presented for both populations.
All controlled clinical trials performed during premarketing development (except one fixed dose study) used a titration design. Consequently, it was impossible to adequately evaluate the effects of a given dose on the incidence of adverse events.

Adverse Reactions Associated with Discontinuation of Treatment

Early Parkinson's Disease: Approximately 12% of 388 patients treated with MIRAPEX and 11% of 235 patients treated with placebo discontinued treatment due to adverse events. The events most commonly causing discontinuation of treatment were related to the nervous system, namely hallucinations (3.1% on MIRAPEX vs 0.4% on placebo), dizziness (2.1% on MIRAPEX vs 1.0% on placebo), somnolence (1.6% on MIRAPEX vs 0% on placebo), headache and confusion (1.3% and 1.0%, respectively, on MIRAPEX vs 0% on placebo), and to the gastrointestinal system (nausea 12.1% on MIRAPEX vs 0.4% on placebo).
Advanced Parkinson's disease: Approximately 12% of 260 patients treated with MIRAPEX and 16% of

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264 patients treated with placebo discontinued treatment due to adverse events. The events most commonly causing discontinuation of treatment were related to the nervous system, namely hallucinations (2.7% on MIRAPEX vs 0.4% on placebo), dyskinesia (1.9% on MIRAPEX vs 0.8% on placebo), dizziness (1.2% on MIRAPEX vs 1.5% on placebo), confusion (1.2% on MIRAPEX vs 2.3% on placebo, and to the cardiovascular system (postural [orthostatic] hypotension (2.3% on MIRAPEX vs 1.1% on placebo).

Most Frequent Adverse Events

Adverse events occurring with an incidence of greater than, or equal to, 10% and listed in decreasing order of frequency, were as follows:

Early Parkinson's Disease: nausea, dizziness, somnolence, insomnia, asthenia and constipation.

Advanced Parkinson's Disease: postural [orthostatic] hypotension, dyskinesia, insomnia, dizziness, hallucinations, accidental injury, dream abnormalities, constipation and confusion.

Incidence of Adverse Events in Placebo Controlled Trials

Table 1 lists treatment-emergent adverse events that were reported in the double-blind, placebo-controlled studies by ≥1% of patients treated with MIRAPEX and were numerically more frequent than in the placebo group. Adverse events were usually mild or moderate in intensity.

The prescriber should be aware that these figures cannot be used to predict the incidence of adverse events in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical studies. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. However, the cited figures do provide the prescribing physician with some basis for estimating the relative contribution of drug and nondrug factors to the adverse-event incidence rate in the population studied.

Table 1: Adverse Events from Placebo-Controlled Early and Adjunct Therapy Studies (Incidence of events ≥ 1% in patients treated with MIRAPEX and numerically more frequent than in patients treated with placebo)

	Early Therapy		Advanced Therapy	
Body System/ Adverse Event	Mirapex N = 388 % occurrence	Placebo N = 235 % occurrence	Mirapex† N = 260 % occurrence	Placebo† N = 264 % occurrence
Body as a Whole				
Asthenia	14	12	10	8
General edema	5	3	4	3
Malaise	2	1	3	2
Reaction unevaluable	2	1	-	-
Fever	1	0	-	-
Chest pain	-	-	3	2
Accidental injury	-	-	17	15
Digestive System				
Nausea	28	18	-	-
Constipation	14	6	10	9
Anorexia	4	2	-	-
Dysphagia	2	0	-	-
Dry Mouth	-	-	7	3
Metabolic & Nutritional System				
Peripheral edema	5	4	2	1
Decreased weight	2	0	-	-
Increased creatine PK	-	-	1	0
Cardiovascular System				
Postural hypotension	-	-	53	48
Nervous System				
Dizziness	25	24	26	25
Somnolence	22	9	9	6
Insomnia	17	12	27	22
Hallucinations	9	3	17	4
Confusion	4	1	10	7
Amnesia	4	2	6	4
Hyperesthesia	3	1	-	-
Dystonia	2	1	8	7
Thinking abnormalities	2	0	3	2
Decreased libido	1	0	-	-
Myoclonus	1	0	-	-
Hypertonia	-	-	7	6
Paranoid reaction	-	-	2	0
Delusions	-	-	1	0
Sleep disorders	-	-	1	0
Dyskinesia	-	-	47	31
Gait abnormalities	-	-	7	5
Dream abnormalities	-	-	11	10
Special Senses				
Vision Abnormalities	3	0	3	1
Accommodation abnormalities	-	-	4	2
Diplopia	-	-	1	0
Urogenital System				
Impotence	2	1	-	-
Urinary frequency	-	-	6	3
Urinary tract infection	-	-	4	3
Urinary incontinence	-	-	2	1
Musculoskeletal System				
Arthritis	-	-	3	1
Twitching	-	-	2	0
Bursitis	-	-	2	0
Myasthenia	-	-	1	0
Respiratory System				
Dyspnea	-	-	4	3
Rhinitis	-	-	3	1
Pneumonia	-	-	2	0
Skin & Appendages				
Skin disorders	-	-	2	1

† Patients received concomitant levodopa

* Patients may have reported multiple adverse experiences during the study or at discontinuation, thus, patients may be included in more than one category.

Other events reported by 1% or more of patients treated with MIRAPEX but reported equally or more frequently in the placebo group were as follows:

Early Parkinson's Disease: Infection, accidental injury, headache, pain, tremor, back pain, syncope, postural hypotension, hypertonia, diarrhea, rash, ataxia, dry mouth, leg cramps, twitching, pharyngitis, sinusitis, sweating, rhinitis, urinary tract infection, vasodilation, flu syndrome, increased saliva, tooth disease, dyspnea, increased cough, gait abnormalities, urinary frequency, vomiting, allergic reaction, hypertension, pruritis, hypokinesia, increased creatine PK, nervousness, dream abnormalities, chest pain, neck pain, paresthesia, tachycardia, vertigo, voice alteration, conjunctivitis, paralysis, accommodation abnormalities, tinnitus, diplopia, and taste perversions.

Advanced Parkinson's Disease: Nausea, pain, infection, headache, depression, tremor, hypokinesia, anorexia, back pain, dyspepsia, flatulence, ataxia, flu syndrome, sinusitis, diarrhea, myalgia, abdominal pain, anxiety, rash, paresthesia, hypertension, increased saliva, tooth disorder, apathy, hypotension, sweating, vasodilation, vomiting, increased cough, nervousness, pruritus, hyperesthesia, neck pain, syncope, arthralgia, dysphagia, palpitations, pharyngitis, vertigo, leg cramps, conjunctivitis, and lacrimation.

Adverse Events: Relationship to Age, Gender, and Race

Among the treatment-emergent adverse events in patients treated with MIRAPEX, hallucinations appeared to exhibit a positive relationship to age. No gender-related differences were observed. Only a small percentage (4%) of patients enrolled were non-Caucasian, therefore, an evaluation of adverse events related to race is not possible.

Other Adverse Events Observed During All Phase 2 and 3 Clinical Trials

MIRAPEX has been administered to 1,715 subjects during the premarketing development program, 782 of whom participated in double-blind, controlled studies. During these trials, all adverse events were recorded by the clinical investigators using terminology of their own choosing. To provide a meaningful estimate of the proportion of individuals having adverse events, similar types of events were grouped into a smaller number of standardized categories using modified COSTART dictionary terminology. These categories are used in the listing below. The events listed below occurred in less than 1% of the 1,715 subjects exposed to MIRAPEX. All reported events, except those already listed above, are included, without regard to determination of a causal relationship to MIRAPEX.

Events are listed within body-system categories in order of decreasing frequency.

Body as a whole: fever, enlarged abdomen, rigid neck, no drug effect.

Cardiovascular system: palpitations, angina pectoris, atrial arrhythmia, peripheral vascular disease.

Digestive system: tongue discoloration, GI hemorrhage, fecal incontinence.

Endocrine system: diabetes mellitus.

Hemic & lymphatic system: ecchymosis.

Metabolic & nutritional system: gout.

Musculoskeletal system: bursitis, myasthenia.

Nervous system: apathy, libido decrease, paranoid reaction, akinesia, coordination abnormalities, speech disorder, hyperkinesia, neuralgia.

Respiratory system: voice alteration, asthma, hemoptysis.

Skin & appendages: skin disorder, herpes simplex.

Special senses: tinnitus, taste perversion, otitis media, dry eye, ear disorder, hemianopia.

Urogenital system: urinary incontinence, dysuria, prostate disorder, kidney calculus.

Post-Marketing Experience

Insomnia and peripheral edema have been reported.

Patients treated with MIRAPEX have rarely reported suddenly falling asleep while engaged in activities of daily living, including operation of motor vehicles which has sometimes resulted in accidents (see Warnings).

Post marketing experience suggests MIRAPEX may be associated with increase or decrease of libido.

DOSAGE AND ADMINISTRATION

MIRAPEX (pramipexole dihydrochloride) should be taken three times daily.

In all clinical studies, dosage was initiated at a subtherapeutic level to avoid orthostatic hypotension and severe adverse effects. MIRAPEX should be titrated gradually in all patients. The dosage should be increased to achieve maximal therapeutic effect, balanced against the principal adverse reactions of dyskinesia, nausea, dizziness and hallucinations.

Initial Treatment

Dosages should be increased gradually from a starting dose of 0.375 mg/day given in three divided doses and should not be increased more frequently than every 5 to 7 days. A suggested ascending dosage schedule that was used in clinical studies is shown in the following table:

Ascending-Dose Schedule of MIRAPEX

Week	Dosage (mg)	Total Daily Dose (mg)
1	0.125 tid	0.375
2	0.25 tid	0.75
3	0.50 tid	1.50
4	0.75 tid	2.25
5	1.00 tid	3.00
6	1.25 tid	3.75
7	1.50 tid	4.50

The maximal recommended dose of MIRAPEX is 4.5 mg per day. MIRAPEX is not recommended at the 6 mg per day dose since the incidence of some adverse reactions is higher.

Maintenance Treatment

MIRAPEX was effective and well-tolerated over a dosage range of 1.5 to 4.5 mg/day, administered in equally divided doses three times per day, as monotherapy or in combination with levodopa (approximately 800 mg/day). In a fixed-dose study in patients with early Parkinson's disease, MIRAPEX at doses of 3, 4.5 and 6 mg/day was not shown to provide any significant benefit beyond that achieved at a daily dose of 1.5 mg/day. For individual patients who have not achieved efficacy at 1.5 mg/day, higher doses can result in additional therapeutic benefit.

When MIRAPEX is used in combination with levodopa, a reduction of the levodopa dosage should be considered. In the controlled study in advanced Parkinson's disease, the dosage of levodopa was reduced by an average of 27% from baseline.

Patients with Renal Impairment

Since the clearance of MIRAPEX is reduced in patients with renal impairment (see Pharmacokinetics), the following dosage recommendation should be considered:

MIRAPEX Dosage in Renal Impairment

Renal Status	Starting Dose (mg)	Maximum Dose (mg)
Mild Impairment (creatinine Cl > 60 mL/min)	**0.125 tid**	**1.5 tid**
Moderate Impairment (creatinine Cl = 35 to 59 mL/min)	**0.125 bid**	**1.5 bid**
Severe Impairment (creatinine Cl = 15 to 34 mL/min)	**0.125 qd**	**1.5 qd**
Very Severe Impairment (creatinine Cl < 15 mL/min and hemodialysis patients)	**MIRAPEX has not been adequately studied in this group and its administration to patients with end stage renal disease is not recommended.**	

Discontinuation of Treatment

It is recommended that MIRAPEX be discontinued over a period of one week. However, in some studies, abrupt discontinuation was uneventful.

AVAILABILITY OF DOSAGE FORMS

MIRAPEX (pramipexole dihydrochloride) Tablets are available in bottles of 90 tablets.

0.25 mg: white, oval, scored tablet with "U" twice on one side and "4" twice on the reverse side containing 0.25 mg pramipexole dihydrochloride as pramipexole dihydrochloride monohydrate.

0.5 mg: white, oval, scored tablet with "U" twice on one side and "8" twice on the reverse side containing 0.5 mg pramipexole dihydrochloride as pramipexole dihydrochloride monohydrate.

1.0 mg: white, round, scored tablet with "U" twice on one side and "6" twice on the reverse side containing 1.0 mg pramipexole dihydrochloride as pramipexole dihydrochloride monohydrate.

1.5 mg: white, round, scored tablet with "U" twice on one side and "37" twice on the reverse side containing 1.5 mg pramipexole dihydrochloride as pramipexole dihydrochloride monohydrate.

Reference: 1. Frucht S, et al. Falling asleep at the wheel: Motor vehicle mishaps in persons taking pramipexole and ropinirole. Neurology 1999; 52: 1908-1910.

PRODUCT MONOGRAPH AVAILABLE UPON REQUEST FROM:

Boehringer Ingelheim (Canada) Ltd.,
5180 South Service Road,
Burlington, Ontario, Canada L7L 5H4

Boehringer Ingelheim

Boehringer Ingelheim (Canada) Ltd.
5180 South Service Rd.,
Burlington (Ontario) L7L 5H4
www.boehringer-ingelheim.ca

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PRESCRIBING INFORMATION

Pr Aggrenox® Capsules

(Dipyridamole / Acetylsalicylic Acid)

200 mg Extended Release Dipyridamole / 25 mg Immediate Release Acetylsalicylic Acid (ASA)

THERAPEUTIC CLASSIFICATION

Antiplatelet Agent

CLINICAL PHARMACOLOGY

AGGRENOX was studied in a double-blind, placebo-controlled, 24-month study (European Stroke Prevention Study 2 - ESPS-2)* in which 6602 patients participated. Seventy six percent (76%) had an ischemic stroke and 24% had a transient ischemic attack within three months prior to entry. Mean age of the patients was 66.7 years. The gender disposition was 58.0% male and 42.0% female. Patients were randomized to one of four treatment groups using a 2-by-2 factorial design: AGGRENOX (extended release dipyridamole 200 mg/ASA 25 mg); extended release dipyridamole (ER-DP) 200 mg alone; ASA 25 mg alone; or placebo. Patients received one capsule twice daily (morning and evening). Efficacy assessments included analyses of stroke (fatal or non-fatal) as confirmed by a blinded assessment group, as well as analyses of stroke (fatal or non-fatal) as confirmed by a blinded assessment group, as well as analyses of the combined endpoint of stroke or death. Secondary endpoints were transient ischemic attack (TIA), other vascular (OVE), myocardial infarction (MI) and ischemic events. OVE was defined as a composite of deep venous thrombosis, peripheral arterial occlusion, pulmonary embolism, and retinal vascular occlusion. Ischemic events comprised stroke, MI, and sudden death.

STROKE ENDPOINT

AGGRENOX significantly reduces the risk of stroke by 36.8% compared with placebo ($p<0.001$). Factorial analysis demonstrated that ER-DP reduces the risk of stroke by 18.9% ($p=0.001$) and ASA reduces the risk of stroke by 21.2% ($p<0.001$) when compared to placebo. Therefore, AGGRENOX reduces the risk of stroke by a further 22.1% when compared with ASA ($p=0.008$). The factorial analysis shows that the effect of DP and ASA in AGGRENOX are additive. Nearly twice as many events are avoided with AGGRENOX therapy than with ASA or ER-DP given alone, as compared with placebo. Primary survival analysis found no significant reduction in death either by ASA, DP, or AGGRENOX in patients with a recent ischemic stroke or TIA.

*After publication of ESPS-2, the data was re-analyzed for use with regulatory authorities in North America. The results presented here reflect the results of this re-analysis, which will explain some minor discrepancies between the numerical values reported here and those reported in the publications of this study. The re-analysis did not affect the significance of any of the results.

TABLE 1: SUMMARY OF FIRST STROKE (FATAL OR NON-FATAL): STUDY ESPS-2

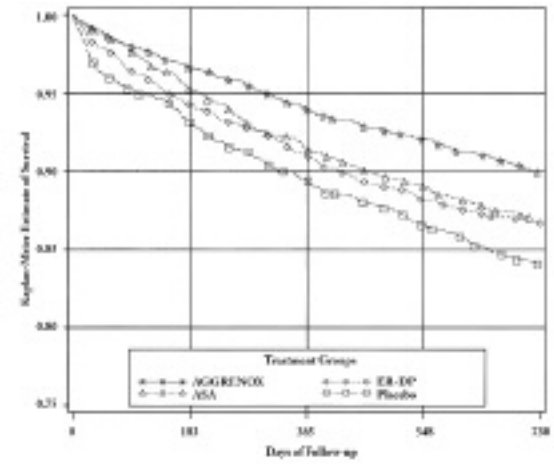
	Total Number of Patients N	Number of Patients with Stroke within 2 Years - N (%)	Kaplan-Meier Stroke- Free Survival at 2 Years % - (95% C.I.)
Factorial Analysis Groups			
ER-DP (AGGRENOX, ER-DP alone)	3304	368 (11.1)	88.3 (87.2, 89.4)
No ER-DP (ASA alone, placebo)	3298	456 (13.8)	85.6 (84.3, 86.8)
ASA (AGGRENOX, ASA alone)	3299	363 (11.0)	88.5 (87.4, 89.6)
No ASA (ER-DP alone, placebo)	3303	461 (14.0)	85.4 (84.1, 86.6)
Individual Treatment Groups (b.i.d.)			
AGGRENOX	1650	157 (9.5)	89.9 (88.4, 91.4)
ER-DP	1654	211 (12.8)	86.7 (85.0, 88.4)
ASA	1649	206 (12.5)	87.1 (85.4, 88.7)
Placebo	1649	250 (15.2)	84.1 (82.2, 85.9)

	P-Value*	Risk Reduction (%) at 2 Years	Odds Reduction (%) (95% C.I.)
Factorial Analysis Groups			
ER-DP vs. No ER-DP	0.001	18.9	22 (9, 32)
ASA vs. No ASA	<0.001	21.2	24 (12, 34)
ER-DP x ASA Interaction	0.850	-	-
Pairwise Treatment Groups			
AGGRENOX vs. placebo	<0.001	36.8	41 (27, 52)
ER-DP vs. placebo	0.036	16.5	18 (0, 33)
ASA vs. placebo	0.009	18.9	20 (3, 34)

* P-values from planned Gehan-Wilcoxon survival analysis.
Note: ER-DP = Extended Release Dipyridamole 400 mg/day; ASA = Acetylsalicylic Acid 50 mg/day.

The stroke-free survivor outcome for AGGRENOX was superior to those for placebo, ER-DP alone, and ASA alone throughout the follow-up period (Figure 1).

FIGURE 1: FIRST STROKE (FATAL OR NON-FATAL): STUDY ESPS-2 KAPLAN-MEIER SURVIVOR FUNCTION FOR EACH TREATMENT GROUP



Note: ER-DP = Extended Release Dipyridamole 200 mg b.i.d.; ASA = Acetylsalicylic Acid 25 mg b.i.d.
Note: The dosage regimen for all treatment groups is b.i.d.

SECONDARY ENDPOINTS

Two separate secondary endpoints - TIA and OVE - strongly substantiated the individual and additive effectiveness of DP and ASA, as previously demonstrated by the primary analyses of stroke. Although the patient number with OVE was very small in all treatment groups, it was demonstrated that both DP and ASA produced significant reductions in TIA and OVE, and had additive effects in combination. Compared with placebo, AGGRENOX capsules reduced the (adjusted) odds of 1 TIA by 40% and reduced the odds of OVE by 62%. DP and ASA also produced significant reductions in the protocol-specified secondary ischemic events endpoint, and these effects were additive in AGGRENOX. The results were primarily driven by the dominant stroke component. For acute MI, the only suggested effect was a 21% (95% C.I. -8% to 42%) odds reduction on ASA vs. no ASA.

INDICATIONS AND CLINICAL USE

AGGRENOX is indicated for the prevention of stroke in patients who have had a previous stroke or a transient ischemic attack (TIA).

CONTRAINDICATIONS

AGGRENOX is contraindicated in patients with hypersensitivity to dipyridamole, ASA or any of the other product components. Due to the ASA component, AGGRENOX is also contraindicated in patients with known allergy to nonsteroidal anti-inflammatory drug products and in patients with the syndrome of asthma, rhinitis, and nasal polyps.

WARNINGS

ALCOHOL WARNING: Patients who consume three or more alcoholic drinks every day should be counseled about the bleeding risks involved with chronic, heavy alcohol use while taking AGGRENOX, due to the ASA component.

PEPTIC ULCER DISEASE: Patients with a history of active peptic ulcer disease should avoid using AGGRENOX, which can cause gastric mucosal irritation, and bleeding, due to the ASA component.

PEDIATRIC USE: Safety and effectiveness of AGGRENOX in pediatric patients has not been studied. Therefore, AGGRENOX should not be used in pediatric patients.

PREGNANCY: There are no adequate and well-controlled studies of AGGRENOX in pregnant women. Because animal reproduction studies are not always predictive of human response, AGGRENOX should be given during the first two trimesters of pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus. Due to the ASA component, AGGRENOX should not be prescribed during the third trimester of pregnancy.

PRECAUTIONS

GENERAL

AGGRENOX should be used with caution in patients with severe coronary artery disease (e.g., unstable angina or recently sustained myocardial infarction), due to the vasodilatory effect of the dipyridamole component. Chest pain may be aggravated in patients with underlying coronary artery disease who are receiving dipyridamole. Patients being treated with AGGRENOX should not receive additional intravenous dypyridamole. If pharmacological stress testing with intravenous dipyridamole for coronary artery disease is considered necessary, then AGGRENOX should be discontinued twenty-four hours prior to testing, otherwise the sensitivity of the intravenous stress test could be limited.

For stroke or TIA patients for whom ASA is indicated to prevent recurrent myocardial infarction (MI) or angina pectoris, the dose of ASA in AGGRENOX has not been proven to provide adequate treatment for these cardiac indications.

ASA should not be used in children or teenagers for viral infections, with or without fever, because of the risk of Reye's syndrome with concomitant use of ASA in certain viral illnesses.

Due to the ASA component, AGGRENOX should be avoided in patients with severe renal failure (glomerular filtration rate less than 10 mL/min) and in patients with severe hepatic insufficiency.

AGGRENOX should be used with caution in patients with inherited (hemophilia) or acquired (liver disease or vitamin K deficiency) bleeding disorders, due to the fact that even low doses of ASA can inhibit platelet function leading to an increase in bleeding time.

GI side effects include stomach pain, heartburn, nausea, vomiting, diarrhea, and gross GI bleeding. Although minor upper GI symptoms, such as dyspepsia, are common and can occur anytime during therapy, physicians should remain alert for signs of ulceration and bleeding, even in the absence of previous GI symptoms. Physicians should inform patients about the signs and symptoms of GI side effects and what steps to take if they occur.

CARCINOGENESIS AND IMPAIRMENT OF FERTILITY

Carcinogenesis: In carcinogenicity studies in rats and mice with the combination of dipyridamole and ASA at the ratio of 1:6 over a period of 125 and 105 weeks respectively, no significant tumorigenic effect was observed at maximum doses of 450 mg/kg (corresponding to a share of 75 mg/kg of dipyridamole, 9 times the maximum recommended daily human dose for a 50 kg person on a mg/kg basis [or 1.5-2.1 times on a mg/m^2 basis]), and 375 mg/kg ASA, 375 times the maximum recommended daily human dose for a 50 kg person on a mg/kg basis (or 58-83 times on a mg/m^2 basis).

Fertility: Fertility studies with dipyridamole revealed no evidence of impaired fertility in rats at oral dosages of up to 1,250 mg/kg, 156 times the maximum recommended human dose on a mg/kg basis for a 50 kg person (or 35 times on a mg/m^2 basis). ASA inhibits ovulation in rats.

NURSING MOTHERS

Dipyridamole and ASA are excreted in human breast milk in low concentrations. Therefore, caution should be exercised when AGGRENOX is administered to a nursing woman.

LABORATORY TESTS

ASA has been associated with elevated hepatic enzymes, blood urea nitrogen and serum creatinine, hyperkalemia, proteinuria and prolonged bleeding time. Over the course of the 24-month study (ESPS-2), patients treated with AGGRENOX showed a decline (mean change from baseline) in hemoglobin of 0.25 g/dl, hematocrit of 0.75%, and erythrocyte count of 0.13 x 10^6/mm^3.

DRUG INTERACTIONS

Adenosine: Dipyridamole has been reported to increase the plasma levels and cardiovascular effects of adenosine. Adjustment of adenosine dosage may be necessary.

Cholinesterase inhibitors: The dipyridamole component of AGGRENOX may counteract the anticholinesterase effect of cholinesterase inhibitors, thereby potentially aggravating myasthenia gravis.

The following drug interactions are associated with the ASA component of AGGRENOX:

Angiotensin converting enzyme (ACE) inhibitors: Due to the indirect effect of the ASA component on the renin-angiotensin conversion pathway, the hyponatremic and hypotensive effects of ACE inhibitors may be diminished by concomitant administration of AGGRENOX.

Acetazolamide: Due to the ASA component, concurrent use of AGGRENOX and acetazolamide can lead to high serum concentrations of acetazolamide (and toxicity) due to competition at the renal tubule for secretion.

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Anticoagulant therapy (heparin and warfarin): Patients on anticoagulation therapy are at increased risk for bleeding because of drug-drug interactions and effects on platelets. ASA can displace warfarin from protein binding sites, leading to prolongation of both the prothrombin time and the bleeding time. The ASA component of AGGRENOX can increase the anticoagulant activity of heparin, increasing bleeding risk.
Anticonvulsants: The ASA component of AGGRENOX can displace protein-bound phenytoin and valproic acid, leading to a decrease in the total concentration of phenytoin and an increase in serum valproic acid levels.
Beta blockers: The hypotensive effects of beta blockers may be diminished by the concomitant administration of AGGRENOX due to inhibition of renal prostaglandins by ASA, leading to decreased renal blood flow and salt and fluid retention.
Diuretics: The effectiveness of diuretics in patients with underlying renal or cardiovascular disease may be diminished by the concomitant administration of AGGRENOX due to inhibition of renal prostaglandins by ASA, leading to decreased renal blood flow and salt and fluid retention.
Methotrexate: The ASA component of AGGRENOX can inhibit renal clearance of methotrexate, leading to bone marrow toxicity, especially in the elderly or renally impaired.
Nonsteroidal anti-inflammatory drugs (NSAIDs): Due to the ASA component, the concurrent use of AGGRENOX with other NSAIDs may increase bleeding or lead to decreased renal function.
Oral hypoglycemics: AGGRENOX may increase the effectiveness of oral hypoglycemic drugs, leading to hypoglycemia.
Uricosuric agents (probenecid and sulfinpyrazone) and natriuretic agents: The ASA component of AGGRENOX antagonizes the uricosuric action of uricosuric agents. ASA decreased the natriuretic effect of spironolactone in healthy volunteers.
Ibuprofen: The concomitant administration of ibuprofen in healthy volunteers shortened the platelet aggregation inhibitory effect of ASA.

ADVERSE REACTIONS

A 24-month, multicenter, double-blind, randomized study (ESPS-2) was conducted to compare the efficacy and safety of AGGRENOX with placebo, extended release dipyridamole alone and ASA alone. The study was conducted in a total of 6,602 male and female patients who had experienced a previous ischemic stroke or transient ischemia of the brain within three months prior to randomization.
Table 2 presents the incidence of adverse events that occurred in 1% or more of patients treated with AGGRENOX where the incidence was also greater than those patients treated with placebo. Discontinuation due to adverse events in ESPS-2 was 27.8% for AGGRENOX, 28.2% for extended release dipyridamole, 23.2% for ASA, and 23.7% for placebo.

TABLE 2: INCIDENCE OF ADVERSE EVENTS IN ESPS-2*

	Individual Treatment Group			
Body System/Preferred Term	AGGRENOX	ER-DP Alone	ASA Alone	Placebo
Total Number of Patients	1650	1654	1649	1649
Total Number (%) of Patients With at Least One On-Treatment Adverse Event	1319 (79.9%)	1305 (78.9%)	1323 (80.2%)	1304 (79.1%)
Central & Peripheral Nervous System Disorders				
Headache	647 (39.2%)	634 (38.3%)	558 (33.8%)	543 (32.9%)
Convulsions	28 (1.7%)	15 (0.9%)	28 (1.7%)	26 (1.6%)
Gastro-Intestinal System Disorders				
Dyspepsia	303 (18.4%)	288 (17.4%)	299 (18.1%)	275 (16.7%)
Abdominal Pain	289 (17.5%)	255 (15.4%)	262 (15.9%)	239 (14.5%)
Nausea	264 (16.0%)	254 (15.4%)	210 (12.7%)	232 (14.1%)
Diarrhea	210 (12.7%)	257 (15.5%)	112 (6.8%)	161 (9.8%)
Vomiting	138 (8.4%)	129 (7.8%)	101 (6.1%)	118 (7.2%)
Hemorrhage Rectum	26 (1.6%)	22 (1.3%)	16 (1.0%)	13 (0.8%)
Melena	31 (1.9%)	10 (0.6%)	20 (1.2%)	13 (0.8%)
Hemorrhoids	16 (1.0%)	13 (0.8%)	10 (0.6%)	10 (0.6%)
GI Hemorrhage	20 (1.2%)	5 (0.3%)	15 (0.9%)	7 (0.4%)
Body as a Whole – General Disorders				
Pain	105 (6.4%)	88 (5.3%)	103 (6.2%)	99 (6.0%)
Fatigue	95 (5.8%)	93 (5.6%)	97 (5.9%)	90 (5.5%)
Back Pain	76 (4.6%)	77 (4.7%)	74 (4.5%)	65 (3.9%)
Accidental Injury	42 (2.5%)	24 (1.5%)	51 (3.1%)	37 (2.2%)
Malaise	27 (1.6%)	23 (1.4%)	26 (1.6%)	22 (1.3%)
Asthenia	29 (1.8%)	19 (1.1%)	17 (1.0%)	18 (1.1%)
Syncope	17 (1.0%)	13 (0.8%)	16 (1.0%)	8 (0.5%)
Psychiatric Disorders				
Amnesia	39 (2.4%)	40 (2.4%)	57 (3.5%)	34 (2.1%)
Confusion	18 (1.1%)	9 (0.5%)	22 (1.3%)	15 (0.9%)
Anorexia	19 (1.2%)	17 (1.0%)	10 (0.6%)	15 (0.9%)
Somnolence	20 (1.2%)	13 (0.8%)	18 (1.1%)	9 (0.5%)
Musculo-Skeletal System Disorders				
Arthralgia	91 (5.5%)	75 (4.5%)	91 (5.5%)	76 (4.6%)
Arthritis	34 (2.1%)	25 (1.5%)	17 (1.0%)	19 (1.2%)
Arthrosis	18 (1.1%)	22 (1.3%)	13 (0.8%)	14 (0.8%)
Myalgia	20 (1.2%)	16 (1.0%)	11 (0.7%)	11 (0.7%)
Respiratory System Disorders				
Coughing	25 (1.5%)	18 (1.1%)	32 (1.9%)	21 (1.3%)
Upper Respiratory Tract Infection	16 (1.0%)	9 (0.5%)	16 (1.0%)	14 (0.8%)
Cardiovascular Disorders, General				
Cardiac Failure	26 (1.6%)	17 (1.0%)	30 (1.8%)	25 (1.5%)
Platelet, Bleeding & Clotting Disorders				
Hemorrhage NOS	52 (3.2%)	24 (1.5%)	46 (2.8%)	24 (1.5%)
Epistaxis	39 (2.4%)	16 (1.0%)	45 (2.7%)	25 (1.5%)
Purpura	23 (1.4%)	8 (0.5%)	9 (0.5%)	7 (0.4%)
Any Bleeding**	144 (8.7%)	77 (4.7%)	135 (8.2%)	74 (4.5%)
Severity of bleeding:***				
Mild	84 (5.1%)	53 (3.2%)	82 (5.0%)	52 (3.2%)
Moderate	33 (2.0%)	18 (1.1%)	33 (2.0%)	15 (0.9%)
Severe	23 (1.4%)	4 (0.2%)	19 (1.2%)	5 (0.3%)
Fatal	4 (0.2%)	2 (0.1%)	1 (0.1%)	2 (0.1%)
Neoplasm				
Neoplasm NOS	28 (1.7%)	16 (1.0%)	23 (1.4%)	20 (1.2%)
Red Blood Cell Disorders				
Anemia	27 (1.6%)	16 (1.0%)	19 (1.2%)	9 (0.5%)

* Reported by >1% of patients during AGGRENOX treatment where the incidence was greater than those treated with placebo.
** Bleeding at any site, reported during follow-up and within 15 days after eventual stroke or treatment cessation.
*** Severity of bleeding: mild = requiring no special treatment; moderate = requiring specific treatment but no blood transfusion; severe = requiring blood transfusion.
Note: ER-DP = Extended Release Dipyridamole 400 mg/day; ASA = Acetylsalicylic Acid 50 mg/day.
Note: The dosage regimen for all treatment groups is b.i.d.
Note: NOS = not otherwise specified

Rare Adverse Reactions:

Adverse reactions that occurred in less than 1% of patients treated with AGGRENOX in the ESPS-2 study and that were medically judged to be possibly related to either dipyridamole or ASA are listed below.
Body as a Whole: allergic reaction, fever
Cardiovascular: hypotension, flushing
Central Nervous System: coma, dizziness, paraesthesia
Gastrointestinal: gastritis, ulceration and perforation
Hearing & Vestibular Disorders: tinnitus, and deafness. Patients with high frequency hearing loss may have difficulty perceiving tinnitus. In these patients, tinnitus cannot be used as a clinical indicator of salicylism
Heart Rate and Rhythm Disorders: tachycardia, palpitation, arrhythmia, supraventricular tachycardia
Liver and Biliary System Disorders: cholelithiasis, jaundice, abnormal hepatic function
Metabolic & Nutritional Disorders: hyperglycemia, thirst
Platelet, Bleeding and Clotting Disorders: hematoma, gingival bleeding, cerebral hemorrhage, intracranial hemorrhage, subarachnoid hemorrhage
Note: There was one case of pancytopenia recorded in a patient within the AGGRENOX treatment group, from which the patient recovered without discontinuation of AGGRENOX.
Psychiatric Disorders: agitation
Reproductive: uterine hemorrhage
Respiratory: hypernea, asthma, bronchospasm, hemoptysis, pulmonary edema
Special Senses: taste loss
Skin and Appendages Disorders: pruritus, urticaria
Urogenital: renal insufficiency and failure, hematuria

POST-MARKETING EXPERIENCE

The following is a list of additional adverse reactions that have been reported either in the literature or are from post-marketing spontaneous reports for either dipyridamole or ASA.
Body as a Whole: hypothermia
Cardiovascular: angina pectoris, worsening of symptoms of coronary heart disease
Central Nervous System: cerebral edema
Fluid and Electrolyte: hyperkalemia, metabolic acidosis, respiratory alkalosis
Gastrointestinal: pancreatitis, Reyes Syndrome
Hearing and Vestibular Disorders: hearing loss
Hypersensitivity: acute anaphylaxis, laryngeal edema
Liver and Biliary System Disorders: hepatitis, incorporated into gallstones
Musculoskeletal: rhabdomyolysis
Metabolic & Nutritional Disorders: hypoglycemia, dehydration
Blood, Platelet, Bleeding and Clotting Disorders: prolongation of the prothrombin time, prolongation of bleeding time, increased bleeding during and after surgery, disseminated intravascular coagulation, coagulopathy, thrombocytopenia
Reproductive: prolonged pregnancy and labor, stillbirths, lower birth weight infants, antepartum and postpartum bleeding
Respiratory: tachypnea
Skin and Appendages Disorders: rash, alopecia, angioedema
Urogenital: interstitial nephritis, papillary necrosis, proteinuria

Laboratory Changes

Over the course of the 24-month study (ESPS-2), patients treated with AGGRENOX showed a decline (mean change from baseline) in hemoglobin of 0.25 g/dl, hematocrit of 0.75%, and erythrocyte count of 0.13 x 10^6/mm^3.

DOSAGE AND ADMINISTRATION

For oral administration. The recommended dose of AGGRENOX is one capsule twice daily, one in the morning and one in the evening, with or without food. The capsules should be swallowed whole without chewing.

AVAILABILITY OF DOSAGE FORMS

AGGRENOX is available as a hard gelatin capsule, with a red cap and an ivory-coloured body, containing yellow extended release pellets incorporating dipyridamole and a round white tablet incorporating immediate-release ASA. The capsule body is imprinted in red with the Boehringer Ingelheim logo and with "01A".
AGGRENOX is supplied in polypropylene tubes containing 60 capsules. Schedule F.

Product Monograph available upon request.

Boehringer Ingelheim

Boehringer Ingelheim (Canada) Ltd.
5180 South Service Rd.,
Burlington (Ontario) L7L 5H4
www.boehringer-ingelheim.ca

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