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34th MEETING OF THE CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES

PROGRAM and ABSTRACTS

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34TH MEETING OF THE CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES

JUNE 15-19, 1999

EDMONTON, ALBERTA

PROGRAM AND ABSTRACTS

TUESDAY 15 JUNE 1999

NEUROBIOLOGY REVIEW COURSE

Chair: Garth Bray

Multiple Sclerosis
Chemokines in Demyelinating Diseases ..... *Robert B Bell*
Imaging Techniques –
Neuropathology *in vivo* ..... *Donald W Paty*
Peripheral Neuropathies
Neurobiology of Peripheral Nerve ..... *Jack W Griffin*
Diabetic Neuropathy –
Pathogenesis and Treatment ..... *Douglas W Zochodne*
Functional Recovery after CNS Injury
Spinal Cord Injury ..... *Keir G Pearson*
Cerebral Injury ..... *Bryan E Kolb*
Brain Tumor Biology
Basic Principles ..... *Joan J Turner*
Gene Therapy Strategies for Brain Tumours:
Immunogene Therapy ..... *Ken C Petruk*

ALS STRATEGIES FOR QUALITY LIFE/QUALITY CARE

Chair: Marek Gawel

What is ALS? ..... *Marek Gawel*
Progress in treatment/Hope in research ..... *TBA*
The ALS Society and its role ..... *Suzanne Lawson,*
.....*Mary Hatcher, Diane Bedard*
Panel: Coping with the physical challenges of ALS .... *TBA*
Panel: Living life fully with ALS –
Taking charge of life ..... *Michael Strong*
Discussion Groups for Learning from each other
Group 1: Physicians and other Health Professionals
Group 2: Persons with ALS
Group 3: Families and Caregivers

UNUSUAL MOVEMENT DISORDERS VIDEO SESSION

Chairs: Wayne Martin and Doug Hobson

CLINICAL EPILEPSY VIDEO SESSION

Chair: Richard McLachlan

A uniquely instructive case ..... *Mary Anne Lee*
Conundrums in childhood ..... *Joseph Dooley*
Nocturnal spells ..... *Alan Guberman*
When is a seizure not a seizure? ..... *Richard McLachlan*

WEDNESDAY 16 JUNE 1999

MEDICOLEGAL ISSUES IN NEUROLOGY & NEUROSURGERY

Chairs: Oksana Suchowersky, William Tucker,
The physician's role in
personal injury claims .....*Bill Bielby*
(CMPA) (Toronto, ON)
Questions and discussion
Mock Trial
Examination in chief .....*Simon Jones*
(Bennett Jones – Law Firm)
Cross-examination of expert witness .....*Rose Carter*
(Bennett Jones – Law Firm)
Questions and discussion
Pitfalls in preparing the
medico-legal report .....*Bill Bielby, William Tucker*

SPINAL INSTRUMENTATION

Chair: Michael Fehlings

Review of learning objectives ..... *Michael G. Fehlings*
Lectures and Panel Discussion (each lecture will last 20 minutes and be followed by a 10 minute case-oriented panel discussion moderated by Michael G. Fehlings)

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Anatomy and biomechanics of the lumbar spine including anterior surgical approaches ..... *R. John Hurlbert*
Classification and management of lumbar fractures ..... *Ben Guiot*
Evaluation of degenerative low back pain: is there a role for fusion cages? ..... *Richard Fox*
Evaluation and management of lumbar spine deformity including degenerative scoliosis and spondylolisthesis ..... *Sanjay Rao*
Image guided spine surgery ..... *Michael G. Fehlings*
Hands-on sessions with image guided spine surgery systems – Hands-on workshop with cadaver instruction (pedicle screw systems and fusion cages will be emphasized

Future and Current Roles of Intraoperative Brain Imaging

Chair: Ken Petruk

Introduction ..... *Ken Petruk*
Image guidance for brain tumor surgery. Intraoperative MRI and ISG Wand Navigation surgical experience ..... *Mark Bernstein*
Neuro-endoscopic surgery overview ..... *Keith Aronyk*
Intraoperative computer assisted navigation system (Vector Vision) for detection and treatment of brain lesions ..... *Matt Wheatley*
Intraoperative Magnetic Resonance Imaging – development and clinical application
Discussion/Question Period ..... *Garnett Sutherland*

The Triptans in Migraine Therapy

Chair: Werner Becker

What's new in migraine pathophysiology ..... *Jose Antonio Terron*
Symptomatic migraine treatment: where do the triptans fit in? ..... *R Allan Purdy*
When a triptan is indicated, which one to prescribe when? ..... *Marek Gawel*
Are the triptans cost effective therapy? ..... *Werner Becker*
Case studies, symptomatic migraine therapy ..... *Gordon Robinson*
Migraine treatment: What does the future hold? *Scott Meckling*

Source Localization in Focal Epilepsy

Chair: George Elleker

EEG and epileptogenic focus localization .... *Warren Blume*
Computer detection of epileptiform EEG abnormalities ..... *Jean Gottman*
Analysis of digital EEG by voltage topography and dipole models ..... *John Ebersole*
Source modeling for epilepsy evaluation ..... *Zole Koles*
EEG source characterization in Rolandic epilepsy ..... *Peter KH Wong*
Pre-surgical evaluation of pediatric seizure disorders with magnetoencephalography (MEG) ..... *Hiroshi Otusbo*

Controversies in Neurocritical Care

Chairs: Jeanne Teitelbaum, Bryan Young

Electrophysiology in the ICU – Seizure detection by continuous monitoring – "the raw and automated EEG" ..... *John Ebersole*
Withdrawal of care in patients with severe neurologic illness: who decides? Are there laws or tests that can help guide the physician? .. *Mark Heule*
Status epilepticus, a look at differing approaches ..... *Eelco Wyjdycks*
Sedation and paralysis in the ICU ..... *Douglas Zochodne*
Aggressive management of massive stroke ..... *Alastair Buchan*

Electrophysiological Assessment of the Proximal Peripheral Nervous System

Chair: George Elleker

Anatomy review – nerve roots and spinal column, brachial and lumbosacral plexuses ..... *Valerie Cwik*

Radiculopathics

Electrodiagnostic techniques ..... *Andrew Eisen*
Neuroimaging ..... *TBA*
Advances in neurosurgical management ..... *John Hurlbert*

Plexopathies

Electrodiagnostic techniques ..... *Asa Wilbourn*
Imaging ..... *TBA*
Brachial plexus surgery ..... *Richard Moulton*

But what can you do for children with Cerebral Palsy?

Chair: Joe M. Watt

Epidemiology and etiology of cerebral palsy ..... *Charlene Robertson*
"The phenomenon" of cerebral palsy ..... *Peter Rosenbaum*

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Dorsal selective rhizotomy and Baclofen pump in the treatment of spasticity in cerebral palsy .... *Paul Steinbok*
Case presentation and panel discussion *Peter Rosenbaum, ...Marc Moreau , Charlene Robertson, Joe Watt*

Management Issues in Epilepsy

Chair: Mano Javidan

Seizures in ICU ..... *Bryan Young*
Seizure prophylaxis after head injury/surgery .. *Richard Desbiens*
Encephalitis and seizures ..... *Mark Sadler*
Stopping anti-epileptic medications ..... *Jack Schneiderman*
Update on the Ketogenic diet ..... *Elaine Wirrell*
When to consider epilepsy surgery ..... *Mano Javidan*
Vagus nerve stimulation for epilepsy ... *Richard McLachlan*

Thursday 17 June 1999

Meet the Expert Breakfast: Neurosurgery

Andr Olivier (Montreal) and ***Joseph C. Maroon*** (Pittsburgh, USA

Plenary Session I

Chairs: Neelan Pillay, Falah Maroun

Speaker of the Royal College of Physicians and Surgeons of Canada, Neurology,
Turbulence and carotid artery disease ..... *Henry Barnett*
Neurology: Richardson Lecture
Peripheral neuropathy ..... *Jack Griffin*
KG McKenzie Prize Paper in
Clinical Neuroscience Research ..... *Yashail Vora*
Herbert Jasper Prize Paper ..... *K.M. Cahn*
Canadian Society of Clinical Neurophysiologists Guest Lecture, EEG in the 21st Century ..... *John Ebersole*

Industry Course

Exhibit Hall and Poster Sessions

Neurology Debate

Moderator: Wayne Martin

Treatment of early Parkinson's disease: Levodopa vs. dopamine agonists .....*Donald Calne, Anthony Lang*

Plenary Sessions

Oral Platform Sessions

Friday 18 June 1999

Exhibit Hall and Poster Sessions

Meet the Expert Breakfast: Neurology

Henry Barnett (London, ON)

Oral Platform Sessions

Neurosurgery Debate

Moderator: Chris Wallace

A Middle Aged Woman with Large Carotid Ophthalmic Anuerysm Causing Visual Failure: Clip or Coil?
Jean Louis Caron (Vascular Neurosurgery,) and Robert Willinsky (Interventional Neuroradiology,

Plenary Session II

Chairs: Neelan Pillay, Falah Maroun

Speaker of the Royal College of Physicians and Surgeons of Canada, Neurosurgery, A neurosurgeon's quest for spiritual, family and physical balance ... *Joseph C Maroon*
Neurosurgery: Penfield Lecture
Where is epilepsy surgery going? Impact of Modern Imaging and Neuronavigation ..... *Andre Olivier*
KG McKenzie Prize Paper in
Basic Neuroscience Research ..... *Lily Angelov*
André Barbeau Prize – Neurology ..... *A. Douen*
President's Prize Paper – Child Neurology ..... *A Kirton*
peaker of the Royal College of Physicians and Surgeons of Canada, Pediatric Neurology Identification of pediatric candidates for epilepsy surgery..... *Elaine Wyllie*

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SATURDAY 19 JUNE 1999

CHILD NEUROLOGY DAY, PEDIATRIC EPILEPSY

Chair: D. Barry Sinclair

Epilepsy surgery in children:
Issues of timing and outcome ..... *Elaine Wyllie*
The genetics of childhood epilepsy ..... *Fred Andermann*
The new antiepileptic drugs ..... *O. Carter Snead*
Cortical dysplasias in childhood epilepsy . *Fred Andermann*
Pediatric epilepsy surgery at the University of Alberta 1988-1998 – What have we learned? ..... *D. Barry Sinclair*
Psychosocial aspects of pediatric epilepsy .. *Thomas Snyder*
Case presentations in childhood epilepsy .... *Mary Connolly*
..... *Lionel Carmant*

BEHAVIOURAL NEUROLOGY

Chair: Andrew Kirk

Frontal lobe deficits ..... *Andrew Kertesz*
Aphasia .....*Morris Freedman*
Agnosia .....*Howard Chertkow*
Neglect .....*Sandra Black*
Constructional impairment ..... *Andrew Kirk*

STROKE

Chair: Stephen Phillips

Session I

Chair: Christopher Wallace

Insulin and its use in focal and global ischemia ..... *Roland Auer*
Epidemiology and treatment of childhood stroke ..... *Gabrielle deVeber*
Antithrombotic therapy for acute ischemic stroke ..... *Gordon Gubitz*

Session II

Chair: Robert Teasell

Homocysteine: a neglected, treatable cause of atherosclerosis ..... *David Spence*
Intermediary metabolism in stroke hypothermia, and aging ..... *Garnette Sutherland*
Efficacy of aphasia therapy ..... *JB Orange*
When is thrombolysis appropriate for acute stroke patients? ..... *Alastair Buchan*

SYMPTOM MANAGEMENT AND CURRENT THERAPIES IN MS

Chair: Luanne Metz

Introduction to the use of touch pads ..... *Luanne Metz*
Management of attacks ..... *Virginia Devonshire*
Case studies (attacks) ..... *Virginia Devonshire*
Symptomatic management in MS ..... *Elliot Frohman*
Disease altering treatments in MS ..... *Dean Wingerchuk*
Case studies (disease altering treatments).... *Dean Wingerchuk*

DEMENTIA, TREATMENT AND ETHICS

Chair: David Hogan

New drugs for Alzheimer's ..... *Howard Feldman*
Making choices – Which drugs? ..... *David Hogan*
Who is going to pay? ..... *Jeffrey A. Johnson*

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ABSTRACTS

PRIZE PAPER PRESENTATIONS

Herbert Jasper Prize

K.G. McKenzie Prize in Basic Neuroscience Research

K.G. McKenzie Prize in Clinical Neuroscience Research

President's Prize

ORAL PLATFORM SESSIONS

Thursday, June 17, 1999

Friday, June 18, 1999

POSTER PRESENTATIONS

Thursday, June 17, 1999

Friday, June 18, 1999

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1999 PRIZE PAPERS

Herbert Jasper Prize

Age Related Changes in Muscle Fatigue Resistance in Humans

K.M. Chan, A.J. Raja, F.J. Strohschein, K. Lechelt (Edmonton, Alberta)

Background: Changes in muscle fatigue resistance with aging are not well understood. The goal of this study was to compare the relative contributions from the muscle and the central nervous system to muscle fatigue resistance in aging.

Methods: Subjects were asked to carry out 90 s of sustained maximal voluntary isometric contraction (MVC) of the thumb. Tetanic tension through stimulation of the median nerve represented the contractile capacity of the thumb muscles. Interpolated doublets delivered to the median nerve during an MVC represented the overall voluntary activation level while transcranial cortical stimulation with an electromagnetic stimulator was used to assess motor output upstream from the corticomotoneuronal pathway.

Results: After the fatiguing exercise, the elderly group's MVC declined by only 29% as opposed to 47% in the younger group ($p<0.01$). The elderly group's greater fatigue resistance was accounted for by increased fatigue resistance at the muscle level as well as in the central nervous system. At least some of the decline in the central motor drive is upstream from the corticomotoneuronal pathway.

Conclusion: This is the first published study that directly demonstrated a change in the central nervous system contribution to muscle fatigue with aging in humans. Given the functional importance of muscle fatigue, further investigations to elucidate its mechanisms and the effectiveness of intervention are needed.

The K.G. McKenzie Prize in Basic Neuroscience Research

Vascular Endothelial Growth Factor (VEGF) Expression and Receptor Inhibition leading to Tumor Regression in NF-1 Neurogenic Sarcomas

Lilyana Angelov, Bodour Salhia, Luba Roncari, Abhijit Guha (Toronto, Ontario)

Tumour angiogenesis is vital for the continued growth of malignant tumours. Expression of Vascular Endothelial Growth Factor (VEGF) by tumour cells, and the paracrine stimulation of its cognate receptors specifically expressed by endothelial cells, is one of the most important positive inducers of tumour angiogenesis. However, the expression and functional importance of VEGF mediated tumour angiogenesis in Neurofibromatosis-1 (NF-1) neurogenic sarcomas, an incurable, common malignant human peripheral nerve tumour subject to local recurrence and systemic metastasis, is not known and is the focus of this study.

Using immunohistochemical methods and computer assisted image analysis, we demonstrated that NF-1 neurogenic sarcomas had tumour vascularity and VEGF expression which were 6.4- and 15-fold higher than normal nerves respectively. The functional relevance of VEGF was further evaluated in vivo with a small molecule inhibitor (SU5416) of VEGFR-2, the main biologically relevant endothelial receptor activated by VEGF. SU5416 reduced the growth of neurogenic sarcoma xenografts by 54.8% ($p<0.02$), compared to vehicle or PBS controls. This anti-tumour effect was secondary to a 2-fold reduction in the number of tumour vessels in the SU5416 treated mice, a 15-fold reduction in tumour cell proliferation, and a 26-fold increase in the apoptotic rate. Hence, anti-angiogenic therapy targeting VEGF such as with SU5416, may be a useful adjuvant therapy to control local growth and metastasis of these presently terminal human neurogenic sarcomas.

The K.G. McKenzie Prize in Clinical Neuroscience Research

The Value of Transcranial Doppler Ultrasonography in the Diagnosis of Cerebral Vasospasm following Aneurysmal Subarachnoid Hemorrhage

Yashail Y. Vora, J. Max Findlay, David E. Steinke, Maria Suarez-Almazor, Michael L. Martin (Edmonton, Alberta)

Background: Transcranial Doppler (TCD) is routinely employed to diagnose cerebral vasospasm following subarachnoid hemorrhage (SAH). Its reliability in individual patients remains unestablished. We correlated TCD velocities with angiographic vasospasm (AV).

Methods: Aneurysmal subarachnoid hemorrhage patients between Jan 1994-May 1997 were retrospectively reviewed. AV on follow-up angiograms was independently graded as non/mild (less than one third narrowing)/moderate (one third to one half narrowing)/severe (more than half narrowing) by two blinded observers. Middle cerebral artery velocities obtained within one day of the angiogram were correlated with AV for the following categories.

Results: 101 patients were included. Interobserver agreement for AV was good (kappa 0.86). The positive predictive value (PPC) of velocities ≥200 cm/s was 87% but only about 50% for the lower velocities despite significant p values. The negative predictive value (NPV) of velocities <120 cm/s was 94% but only about 75% for higher velocities. The likelihood ratios were useful only for velocities <120 cm/s and ≥200 cm/s. 51% of patients fell in the <120 or ≥200 range. The mean Lindegaard ratio was higher with moderate/severe MCA spasm: 2.57 versus 1.71 ($p=0.02$). The sensitivity, specificity, PPV and NPV of Lindegaard ratio >3 were 39%, 96%, 63%

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and 89% respectively. The average highest velocity was higher during hyperdynamic therapy (HT): 150 vs. 129, p<0.001.

Conclusions: Despite significant p values, only the very low or high absolute velocities (<120 or ≥200) proved to be sufficiently useful to guide clinical management in the individual patient. Absolute velocities were of limited use in half the patients. Lindegaard ratios did not add to the information available from absolute velocities alone. Routine HT may artificially elevate absolute velocities.

The President's Prize

Clinical Phenomenology of Secondary Generalized Seizures in Epileptic Children

A. Kirton, H. Darwish, C. vanVelzer, M. Wilson, V. Lange (Calgary, Alberta)

Background: The phenomenology of primary generalized tonic clonic convulsions (PGS) is well described. When partial seizures become secondarily generalized (SGS) it is assumed that the generalized convulsion (GC) is the same.

Hypothesis: The GC with SGS is different from PGS.

Method: CCTV-EEG recordings of 64 SGS events in 13 children were systematically scored. A group of 10 (A) without any MRI lesion were compared to 3 children with neuroimaging proven temporal sclerosis (MTLS). (A) had clinical and EEG features suggesting "focal onset": 1/10 was temporal, 5/10 frontal and 3/10 unilateral. 4 were mentally normal, 5 borderline and 4 moderately handicapped.

Results: Features atypical of PGS were : 8/13 had mouth open, 8/13 did not show fisting of the hands. "Late motor events", occurred in 10/13. These occurred at a mean 30 sec interval, after the last clonic jerk, with sustained EEG suppression. Clonic jerks of face or limbs occurred in 7/10, gross flailing arm movements in 2/10. 3/10 had lip smacking or manual automatisms.

Discussion: 1/10 (A) considered temporal onset, and 3/3 MTLS had mouth closure or repeated opening and closing. 8/10 (A) had sustained mouth open during GC. The late events were described only by Gastaut and Broughton in SGS, but the mechanism is unclear.

Conclusion: In SGS, the GC and its immediate 1 minute aftermath are different than PGS.

Andr Barbeau Prize

Cortical Spreading Depression Selectively Down Regulates Glial Glutamate Transporter Isoforms EAAT1 and EAAT2 from Rat Cerebral Cortex Plasma Membranes

A. Douen, F. Wang, L. Dong, G. Doumit, A. Hakim, M. Hogan, (Ottawa, Ontario)

Background: Preconditioning with cortical spreading depression (CSD) 3 days prior to cerebral ischemia significantly reduces infarction volume. However, the mechanism of this induced neuroprotection is unknown. We investigated whether CSD pretreatment modulates excitatory amino acid transporters (EAAT) in rat cerebral cortex plasma membranes (PM).

Methods: Rats were submitted to unilateral KCl generated CSD waves in the left cortex for 2 h (n = 3) or to sham (n = 3) treatment with NaCl. Rats were sacrificed 3 days following CSD. Cerebral cortices were removed, homogenized and fractionated by differential centrifugation with precipitation of a PM enriched fraction on a 35% sucrose cushion.

Results: Western blot analysis showed that glial EAAT isoforms EAAT1 and EAAT2 were significantly decreased in PM extracted from CSD treated cortex. In contrast, CSD did not affect the subcellular distribution of the neuronal isoform EAAT3. The data were corroborated by semi-quantitative analysis using a computer based imaging device.

Conclusions: CSD down regulates EAAT1 and EAAT2 but not EAAT3 from rat cerebral cortex PM. This down regulation coincides with the period of CSD-induced neuroprotection. Hypoxia-induced reversal of EAAT function has been implicated in glutamate toxicity during ischemia. CSD mediated down regulation of PM EAAT may reduce glutamate efflux from glial cells during ischemia. We speculate that down regulation of EAAT1 and EAAT2 may underlie CSD-induced neuroprotection.

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Oral Presentations

PLENARY SESSION

A-01

Intra-arterial Thrombolysis in Five Patients with Basilar Artery Thrombosis

P.A. Barber, G.M. Klein, M. Hudon, W. Hu, N. Newcommon, A.M. Buchan. (Calgary, Alberta)

Background: Basilar artery thrombosis has a very poor prognosis with a reported mortality of between 80 and 100% when there is angiographic or pathologic confirmation of the diagnosis.

Methods: We report a series of 5 consecutive patients with a clinical diagnosis of this condition treated with intra-arterial thrombolysis (4 patients had i.a.tissue plasminogen activator and the other i.a. urokinase) over a 30 month period. The timing for referral varied widely in this group of patients. Some were referred from outside hospitals and were observed for variable periods on anticoagulant therapy before endovascular treatment was requested. Two patients were comatose, two others had progressive symptoms resulting in ophthalmoplegia and quadriplegia, and the fifth patient had progressive ataxia and ophthalmoplegia. All patients had pre-treatment imaging, either CT scan or MRI of the brain. Duration of symptoms prior to treatment was 5-36 hours.

Results: The age range of the patients treated was 14-73. Angiography confirmed basilar artery thrombosis in all five patients. 4 of the cases had distal basilar artery thrombosis (one being secondary to a basilar artery dissection) and the fifth case a mid basilar artery thrombosis. Thrombolytic therapy resulted in re-canalization of the artery in all five cases. All patients appeared to improve initially, immediately following treatment. One patient deteriorated very quickly and was diagnosed as having had a brainstem hemorrhage. A second patient developed severe cerebellar oedema. Both of these patients died. One patient was left severely disabled. The other 2 patients had good outcomes (Rankin 0,1).

Conclusions: Intra-arterial thrombolysis is a treatment option for basilar artery thrombosis even when treatment is delayed up to 36 hours. While the mortality of this condition can be very high all patients in this series had severe baseline neurological deficits and 2 of the patients were entirely independent following treatment. This series along with many other small case studies supports the effectiveness of this treatment in a condition where there are no other treatment options.

A-02

How Often Does Routine EEG in Children Have a Surprise Result?

P.R. Camfield, C.S. Camfield (Halifax, Nova Scotia)

Background: Routine EEG is requested for many pediatric problems. To assess the utility of EEG we studied how often routine EEG results are correctly predicted from the EEG requisition.

Methods: 500 consecutive initial EEG requests from the IWK Grace Health Centre from 2 time epoques were examined. All EEGs were 16 channel (10-20 electrode system). Based only on the requisition (patient demographics, referring physician, reason for EEG), we coded our prediction of the result and then the actual result. When results were discordant from prediction, judgment was made about potential importance.

Results: Overall, EEG results were correctly predicted in 81%. Prediction for all non-epilepsy reasons were accurate in 91% (n=320) and 96% for paroxysmal non-epileptic events (n=158) but only 63% for epileptic disorders (n=166) ($p<0.0001$). Neurologists ordered 45% of EEGs, pediatricians 32%, GPs17%. Predictions were least accurate for neurologists' requests ($p<0.006$) however, neurologists were more likely to request EEG for epileptic disorders ($p<0.0001$). Age of the child and urban vs rural address did not affect prediction.

Conclusion: Routine pediatric EEG for non-epilepsy reasons is highly predictable and therefore apparently of little value to an experienced clinician. When requested for epilepsy this "ancient" test remains full of surprises.

A-03

Vagus Nerve Stimulation for Intractable Epilepsy - The Canadian Experience

R.S. McLachlan for the Canadian Vagus Stimulation Study Group. (London, Ontario)

Background: Chronic intermittent stimulation of the vagus nerve (VNS) in the neck is a new treatment for intractable epilepsy. We present the early results of VNS from six epilepsy centres in Canada.

Methods: Patients were considered for VNS if 1) seizures continued despite the use of major antiepileptic drugs, 2) epilepsy surgery failed to control seizures or was not considered a viable option and 3) there was not a progressive neurological disorder. A programmable generator was implanted in the chest wall and connected subcutaneously to leads around the left vagus nerve for chronic intermittent electrical stimulation.

Results: Between January-December 1998, 25 patients (M:F=13:12) with an age range 12-48 years (mean 28 years) were implanted. The epilepsy was mainly generalized in seven and partial (+/- secondary generalization) in 19. Mental subnormality was present in nine patients and 13 had previous unsuccessful epilepsy surgery. Short term follow-up (1-12 months) revealed >50% improved seizure control in 11 and no change in 14. Magnet activation successfully aborted seizures in nine patients. Eleven patients were more alert or felt better independent of seizure control. Complications included transient vocal cord paralysis (2), intractable vomiting (1) and painful neck muscle spasm (1). All patients experienced tolerable hoarseness, cough and/or shortness of breath during stimulation.

Conclusion: VNS provides favourable results in a subgroup of patients with intractable epilepsy with few associated adverse events.

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Longterm follow-up and quality of life assessments are underway to further determine the effectiveness of this novel treatment.

A-04

Current Use and Timing of Surgery for Acute Spinal Cord Injury: Multicenter North American Study in 585 Patients

Charles H. Tator, Michael G. Fehlings (Toronto, Ontario)

A multicenter retrospective study was performed in 365 North American centers to examine the use and timing of surgery in the treatment of acute spinal cord injury (SCI). The records of 585 consecutive patients (16 to 75 y) with acute SCI or cauda equine injury who were admitted to the 36 centers within 24 hours of injury over a 9-month period (8/94-4/95) were examined to obtain data on admission variables, methods of diagnosis, use of traction, and surgical variables including type and timing of surgery. Although 100% of patients underwent CT scanning, only 54% underwent MRI and CT myelography was performed in only 6%. Complete neurological injuries (ASIA Grade A) were present in 57.8%. Traction was applied in only 47% of patients with cervical injuries, of which only 42% demonstrated successful decompression by traction. Neurological deterioration occurred in 8.1% of patents after traction. Surgery was performed in 65.4% of patients. The timing of surgery varied widely: less that 24 hours in 23.5% of patients; 25 to 48 hours in 15.8%; 48 to 96 hours in 19.0%; and 5 days or longer in 41.7% of patients. These data indicate that whereas surgery is commonly performed in patients with acute SCI, one-third of the cases are managed nonoperatively, and there is very little agreement on the optimum timing of surgical treatment. The results of this study confirm the need for a randomized controlled trial to determine the optimum timing of surgical decompressive procedure in patient with SCI.

MOVEMENT DISORDERS

B-01

Functional and Anatomical Recovery of the Nigrostriatal Circuitry by Double Grafting of Human Ventral Mesecephalon Cells in the Rodent Model of Parkinson's Disease

M. Hong, I. Mendez (Halifax, Nova Scotia)

Background: Parkinson's Disease (PD) is a hypokinetic neurological disorder resulting from the loss of dopamine (DA) neurons of the nigrostriatal pathway. Although transplantation of fetal tissue into striatal targets is currently in clinical trials with promising results, it has not yet reached a level to become a routine therapeutic option for PD patients. One possibility for limited results is that the ectopic placement of tissue into striatum is not sufficient for complete restoration and that homotopic placement of tissue into the nigra is also required for full recovery. We have previously demonstrated the reconstruction of the nigrostriatal pathway by simultaneous intrastriatal and intranigral transplants of rat fetal tissue but it has not been demonstrated with human tissue.

Methods: To study the functional and anatomical recovery produced by neural transplantation, a microgrefting technique was used to stereotaxically implant human fetal nigral dopaminergic cell suspensions into both the striatum and substantia nigra of female, Wistar rats (200-225 g) with unilateral 6-hydroxydopamine (6-OHDA) lesions of the nigrostriatal DA pathway and immunosuppressed with cyclosporin (10 mg/kg i.p. daily). Analysis of functional recovery was carried out using a video activity monitor to assess locomotor activity and analysis of anatomical recovery was done using tyrosine hydroxylase (TH) immunohistochemistry.

Results: Two weeks after lesioning, a pre-graft amphetamine (5 mg/kg i.p.) challenge induced asymmetric turning behaviour towards the lesioned side of 10.9 ± 1.3 rotations/min over a 60 min observation period (mean (SEM, n=6) which was significantly reduced to 1.1 ± 0.5 rotations/min at 6 weeks following transplantation. TH +'ve cell bodies were seen in grafts both in the striatum and substantia nigra with a dense network of TH+'ve processes within the grafts and projecting between the grafts suggesting restoration of the nigrostriatal pathway.

Conclusions: This study demonstrates for the first time both functional and anatomical restoration of the nigrostriatal pathway by double grafting of human fetal VM tissue in the 6-OHDA rat model of PD.

B-02

Benefits and Risks of Pallidotomy in Parkinson's Disease: The Calgary Experience

M. Walsh, J. Krcek, M.F. Wilkinson, J. Warner, G. Rohs, O. Suchowersky (Calgary, Alberta).

Introduction: Pallidotomy using microelectrode recording technique became a surgical option in the treatment of Parkinson's disease in Calgary in 1996. As a new center for this treatment, we wished to review our complication rate and benefits as compared to other centers.

Material and Methods: 20 patients have undergone this procedure with an additional 2 patients having undergone surgery but no lesioning. A battery of measurements was collected prospectively including total daily "on" and "off" time, Universal Parkinson's Disease Rating Scale (UPDRS) scores in both the "on" and "off" state, Schwab and England scores in both the "on" and "off" states, best and worst Hoehn and Yahr scores, and dyskinesia rating. The scores were collected pre-operative, 1 month, 6 month, 12 month and 24 month post-operatively. Each category was subjected to a one-way ANOVA to determine if there was a statistically significant post-operative change. All charts were reviewed for post-operative complications.

Results: Of the 22 patients undergoing surgery, 9 had mild and transient side effects. The breakdown for these was as follows: dysphagia (4), urinary urgency (2), facial weakness (3),

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memory problems (2), dysarthria (2), pain (1). One patient had an intracerebral hemorrhage post-operatively from which he did not recover despite evacuation. One patient died 3 weeks post-operatively from unrelated causes.

At 1 month, patients had statistically significant improvement in "on" time, (8 hours pre-op vs. 12 hours post-op) "off" time (7 hours pre-op vs. 4 hours post-op), UPDRS Sub-scale III "off" scores (42 pre-op vs. 32 post-op), Schwab and England "off" scores (39 pre-op vs. 59 post-op) and dyskinesia scores (3.8 pre-op vs. 1.6 post-op). Six, 12 and 24 month data is currently being analyzed.

Conclusions: At our center, pallidotomy complication rates were comparable to those reported from other centers. Unilateral pallidotomy significantly improved the measures of disease particularly in the "off" state and dyskinesias. On-time was significantly increased. Pallidotomy using microelectrode technique is a safe and effective procedure in PD.

B-03

Unilateral Pallidotomy Reduces Parkinsonian Pain

C.R. Honey, A.J. Stoessl, J.K.C. Tsui, M. Schulzer and D.B. Calne (Vancouver, British Columbia)

The percentage of patients suffering pain attributable to their PD has been estimated to be between 15-46%. With the increased popularity of the pallidotomy procedure have come anecdotal comments on its ability to reduce pain. We conducted a prospective study to determine if unilateral pallidotomy reduces the pain attributable to PD. Fifty PD patients selected for pallidotomy based on their motor symptoms, were studied. The ventroposterior pallidal target (4-6mm below the intercommissural line, 21-23mm lateral, and 2mm anterior to its midpoint) was confirmed with intraoperative macrostimulation. Patients described the severity of their pain on an ordinal scale (0-10 scale) pre-operatively and at six weeks and one year post-operatively. Organic pain unrelated to PD was excluded. Scores were then analysed by Wilcoxon paired-ranks test with a Bonferroni correction. Descriptive data were also recorded on pain location, quality, and relation to PD symptoms, medications and time of day. PD pain was then grouped into categories based on a modification of Goetz's classification. Twenty-one patients (42%) had pain attributable to their PD. There was a significant reduction in overall pain scores at six weeks ($p<0.001$) and one year ($p=0.001$) following pallidotomy. Various types of PD pain are described and the possible mechanisms for their etiology presented. Unilateral pallidotomy significantly reduces pain attributable to Parkinson's Disease.

B-04

Control of Tremor in Parkinson's Disease and Essential Tremor by Deep Brain Stimulation of the Ventral Intermediate Nucleus (VIM) of the Thalamus

Krishna Kumar, Cory Toth, M. Kelly, (Regina, Saskatchewan)

Background: Thalamic stimulation is a non-ablative procedure which has the advantage of a reversible, non-destructive lesion. In situations where VIM stimulation is required bilaterally, this procedure avoids the complication of cognitive deficit observed in cases of bilateral thalamotomies. We evaluate the beneficial effects of VIM stimulation in patients with tremor refractory to medical therapy.

Methods: We have attempted VIM stimulation in ten tremor-dominant Idiopathic Parkinson's Disease (PD) patients and nine Essential Tremor (ET) patients who were considered to have tremor refractory to medical therapy.

Results: Thirteen patients (7 PD, 6 ET) received unilateral VIM implantation while six patients had staged bilateral VIM implantation (3 PD, 3 ET). PD patients showed a significant improvement in contralateral arm and leg rest tremor and ipsilateral leg rest tremor ($P<0.02$) at a mean follow-up period of 18 months $\pm$ 7 months. Patients with PD did not demonstrate any significant decrease in medication use at follow-up. ET patients demonstrated significant improvement in postural and action tremor in the contralateral arm ($P<0.001$) at follow-up but no significant improvement in the contralateral leg tremor at follow-up. Significant improvements were also seen in ET patients in the Clinical Tremor Rating Scale (CTRS) ($P<0.001$) with respect to several activities of daily living at a mean follow-up of 14 $\pm$ 7 months. Complications consisted of focal seizures in two patients, mild paresthesiae (2), mild dystonia (2), dysarthria (1), and superficial skin infection (1).

Conclusion: Deep brain stimulation is a safe and effective treatment for severe tremor refractory to medications. It is a highly effective, reversible, adaptable, and predictable procedure which is well tolerated even in the elderly and should be considered an alternative to classic thalamotomy.

B-05

MRI and fMRI with Deep Brain Stimulators (DBS): Safety Update

D.J. Mikulis, A.P. Crawley, (Toronto, Ontario)

Purpose: Assess the safety of performing MRI and fMRI in patients with deep brain stimulators (DBS) prior to implantation of pulse generators.

Methods: The primary risk of imaging patients with DBS prior to implantation of the pulse generator, is heating from current deposition at the electrode tip from a closed circuit in which the patient becomes part of a large loop containing the DBS lead. Voltage measurements were performed to investigate the magnetic field gradient contribution to induced voltages in conductive loops during conventional, EPI, and spiral imaging. These were compared with known radiofrequency (rf) induced voltages.

Results: The induced rms voltage in a large loop ($400cm^2$) from rf and gradient contributions was approximately 4 volts resulting in a peak energy deposition adjacent to the electrode of approximately 9 watts/kg.

Conclusion: Deposition of 9 watts of energy per kg of brain tissue poses some risk of injury through heating. This would

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only occur if the stimulator lead and the patient's body form a large low resistance circuit. This can be avoided by passing the stimulator lead out of the back of the scanner bore. To date we have safely scanned > 100 patients with conventional MRI and > 15 patients with fMRI. WARNING - we have not yet tested systems containing implanted pulse generators!

EPILEPSY

C-01

Propagation Pathways of Subdurally Recorded Frontal Lobe Seizures

Warren T. Blume, D. Ociepa (London, Ontario)

Background: To study frontal seizure propagation as recorded by subdural electrode lines in 12 patients with intractable seizures.

Methods: Patients with intractable clinically focal seizures who desire surgical consideration. The epileptogenic zone was undetermined by non-invasive means. Bifrontal subdural lines covered the convexity, mesial and orbital frontal surfaces with 10 mm interelectrode distances. Seizures began anterior to the Rolandic fissure and were fully recorded.

Results: Inter-patient propagation patterns varied considerably. However, intra-patient propagation patterns were stereotyped in 6 of the 7 patients with more than one seizure. Seizures initially propagated to contiguous zones in 8 patients, to homotopic regions in 3, and to contralateral non-homotopic areas in 1. No propagation occurred in 2 patients; seizures of 1 moved from one ipsilateral region to another. Propagation began 5 seconds after onset in 8 (67%) of 12 seizures with propagation. Initial propagation occurred more readily (within 2.75 seconds) in the 4 mesially originating seizures whereas the 6 seizures beginning in the convexity failed to propagate until a median of 13.5 seconds elapsed. Ictal seizures spread to become bilaterally synchronous earlier when a lesion was present and when the seizure originated in the mesial frontal region but neither of these associations achieved clinical significance. A median of 17 seconds elapsed before the seizure discharge became bilaterally synchronous.

Conclusions: Frontal lobe seizures propagate in a stereotypic manner for each patient, but with considerable interpatient variability. Seizures spread initially to contiguous zones, usually after at least 5 seconds of focal ictal activity. This data suggests that frontal lobe seizures propagate in a less explosive manner than reputed.

C-02

Hemispherectomy in Children: Hemidecortication Versus Peri-Insular Hemispherotomy

M.B. Connolly, K. Farrell, J. Kestle (Vancouver, British Columbia)

Background: The precise surgical approach for intractable seizures due to diffuse hemispheric disease is controversial. We describe the outcome in 13 children who underwent hemidecortication or peri-insular hemispherotomy.

Methods: 13 children (8F, 5M) had medically refractory epilepsy due to cortical dysplasia (n=4), hemimegalencephaly (n=2), Sturge-Weber syndrome (n=3), Rasmussen's encephalitis (n=3) and porencephaly (n=1). Seizure onset was from 1 day to 5.5 years. In 10 patients, seizure onset was in the first year of life (5 in the first week). Six patients had infantile spasms and all had partial seizures +/- secondary generalization. The first 6 patients underwent hemidecortication and the subsequent 7 had hemispherotomy.

Results: At mean follow up of 38 months (range 6-67 months), 9 (70%) are seizure free and the remainder are >90% improved. Six patients who underwent peri-insular hemispherotomy and 3 of 6 who had hemidecortication are seizure free. Currently, 4 patients are off medications and 9 are on monotherapy. No patient who underwent hemispherotomy required ventriculoperitoneal shunting in contrast with 3 of 6 who had hemidecortication.

Conclusion: In this small series where follow up is short, seizure outcome was better and complication rate lower in patients who underwent peri-insular hemispherotomy compared with hemidecortication.

C-03

Motor Cortex Mapping by Direct Cortical Stimulation in Pediatric Epilepsy Surgery Candidates

M.B. Connolly, S. Smith, J. Kestle, P. Steinbok (Vancouver, British Columbia)

Background: In patients having epilepsy surgery, identification of the sensori-motor cortex is important when the epileptogenic zone is close to or involves this eloquent cortex. Electrical cortical stimulation is technically more difficult in the immature brain. We describe successful sensori-motor cortex mapping in children using subdural electrodes.

Methods: Nine children with intractable seizures underwent subdural electrode placement in order to define the region of epileptogenicity and its relation to eloquent brain function. They were aged 23 months to 13 years (mean 8 years). MR imaging was normal in 6 children, showed cortical dysplasia in 2 and infarction in 1. In the awake state, median nerve stimulation was performed and cortical stimulation according to the protocol proposed by Jayakar et al. J. Clin Neurophysiol 1992.

Results: A cortical response was obtained on median nerve stimulation in all patients. Motor mapping of the hand, wrist, forearm and shoulder was obtained in all patients, of the face in 4, tongue in 3. Stimulus intensity was 4 to 10 mAmp (mean 6.5) and pulse duration 0.4 to 0.7 msec (mean 0.5). Seizures occurred during motor stimulation in 3 children.

Conclusion: Direct motor cortex stimulation is possible and well tolerated in awake young children.

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C-04

Memory morbidity following temporal lobectomy in children and adults

T.J. Snyder, D.B. Sinclair, K. Aronyk, J.McKean, M. Javidan (Edmonton, Alberta)

Rationale: Temporal lobectomy (TLy) is a common, effective procedure for treating medically refractory temporal lobe epilepsy (TLE) in adults and is being used with increased frequency in children. Postoperative morbidity after TLy in adults includes memory decline, especially verbal memory decline after left TLy. Postoperative neuropsychological assessment of children after TLy has not consistently demonstrated memory morbidity, though the data available is limited by few studies of few subjects with few tests of memory and no direct comparisons between children and adults.

Method: 14 children and 14 adults, matched for side of TLy and age of seizure-onset, underwent pre/post neuropsychological assessments that included tests of memory for verbal and nonverbal information.

Results: 2 (age group) x 2 (TLy focus) x 2 (pre/post) repeated measures ANOVAs conducted on T-scores of separate memory tests showed multiple significant differences according to TLy focus, age group, and verbal vs. nonverbal memory. Children with a left focus had poorer verbal memory than adults pre- and post-TLy.

Conclusions: TLy did not result in memory morbidity in children. Differences in age, functional reserve, pathology, and neural organization probably account for the observed differences in memory morbidity between children and adults.

C-05

Invasive Monitoring in Patients with Medically Intractable Epilepsy

R. Sahjpaul, S. Wiebe, M. Pondal, (London, Ontario)

Background: Electrode designs and specifications for invasive intracranial monitoring have evolved over the years; currently, commercially available depth and subdural electrodes (SDE) are the most commonly used. We have (almost exclusively) used SDE manufactured on-site. Our technique of electrode manufacture and insertion is unique in several respects. A retrospective review of our recent experience forms the basis of this report.

Methods: The epilepsy unit database at London Health Sciences Centre was used to identify 133 consecutive patients who underwent invasive monitoring for medically intractable epilepsy.

Results: Mean age was 29.9 y (SD 11.8, range 6-61 y). Average duration of monitoring was 13.1 days (SD 5.7, range 1-30). 116 patients underwent SDE insertion only and 17 underwent subdural grid plus SDE insertion. There were 3 complications (2.3%). Meningitis, brain abscess, and epidural hematoma occurred in one patient each; no patient suffered permanent neurological sequelae. Minor electrode malfunction occurred in 10 patients (7.5%), additional electrodes were required in 6 (4.5%), and repositioning in 3 patients (2.3%).

Conclusions: Subdural electrodes manufactured on-site are a safe and effective method of chronic invasive monitoring for the vast majority of patients with medically intractable epilepsy.

NEUROMUSCULAR DISEASE

D-01

Phenotypical Kennedy's disease with normal trinucleotide CAG repeats

Markus Weber, and Andrew Eisen (Vancouver, British Columbia)

Background: Kennedy's disease (spino-bulbar muscular atrophy) presents with lower motor neuron weakness, wasting, fasciculations and bulbar involvement. It is frequently associated with diabetes, testicular atrophy and gynecomastia. Absent reflexes and small or absent sensory nerve action potentials (SNAPs) are characteristic.An increased number of trinucleotide CAG repeats is specific for this sex-linked recessive disorder.

Methods: Clinical and neurophysiological data were compared in 12 DNA confirmed patients with Kennedy's disease and in 5 patients with negative DNA testing who were phenotypically indistinguishable from Kennedy's disease.

Results: All of the patients with Kennedy's disease had face fasciculations; this was absent in the 5 patients with negative DNA testing. All other features (fasciculations, tremor, bulbar symptoms, cramps, absent deep tendon jerks, diabetes and gynecomastia) were seen in both groups. Motor conduction studies were normal but sensory nerve action potentials were reduced in size or absent. Needle EMG showed changes characteristic of a chronic neurogenic process. There were no specific EMG findings which distinguished the two groups.

Conclusions: We describe 5 patients with the phenotypical characteristics of Kennedy's disease but negative DNA testing. Facial fasciculations may be specific to Kennedy's disease. The findings raise the possibility that the gene defect in Kennedy's disease acts as a modifier gene rather than being a causative factor.

D-02

Tick Paralysis in Children: Difficulties Differentiating from Guillian Barr Syndrome.

V.V. Vedanarayanan (Jackson, Mississippi)

Background: Tick paralysis is an acute rapidly progressive syndrome, characterized by profound areflexic weakness of cranial and extremity muscles. The clinical presentation is similar to Guillian Barré syndrome and the differentiation from it can be difficult. We are presenting the clinical data and electrophysiologic studies on six children who were treated at our center.

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Patients: Six children were treated for acute tick paralysis in the past 5 years. Five were girls and one was a boy, and their ages ranged from 3 years and 4 months to 5 years and 6 months. The time from onset of symptoms to presentation at the hospital were from 7 to 8 hours to 4 days. In four children it was around 24 hours. The onset of weakness was in the lower limbs in all. Generalized weakness was seen in 3 patients and one experienced paresthesias all over. One child developed bulbar and respiratory failure requiring intubation and mechanical ventilation for 12 hours. All of them were areflexic. The cerebrospinal fluid examination in three children were normal.

The tick was found in emergency room in two patients. Admitting diagnosis of GBS was made in others. Two patients received a course of IVIG in the hospital before the tick was found. All patients made a rapid recovery of strength after removal of the tick. Normal motor strength was seen in 24 hours after tick removal in 4 patients, after 36 hours and 72 hours in one each. All but one remained areflexic at discharge from the hospital.

Electrodiagnostic studies were performed on 4 children. Low amplitude CMAP was seen in 3 patients, and low amplitude SNAP in 2. The conduction velocity was mildly slowed in 2 patients. H reflexes were absent in three patients and preserved in one. The repetitive nerve stimulation studies at slow and fast frequencies showed no abnormalities. Needle examination of the muscles revealed normal spontaneous activity, and reduced motor unit recruitment with normal motor unit morphology. Follow up examination was performed on three patients and they all showed improvement in CMAP and SNAP amplitudes and recovery of H reflex.

Conclusion: The clinical presentation of tick paralysis in children is indistinguishable from GBS. Laboratory studies and electrodiagnostic studies do not help in the differentiation. Hence, in every child who is suspected of suffering from GBS, a careful search of the scalp for ticks should be performed.

D-03

Is the Age of Onset of Myasthenia Gravis Increasing? An Analysis of the Acetylcholine Receptor Antibody Assay Database of the Neuro-immunology Laboratory at UBC.

J. Oger, L. Wang, T. Aziz and H. Feldman (Vancouver, British Columbia)

Background: Myasthenia gravis (MG) preferentially affects 2 subgroups of individuals: young subjects (mostly women) and elderly (women = men). We suspect an increase over time of the proportion of elderly diagnosed with this condition.

Methods: We assay acetylcholine receptor antibodies (AchR Ab) for BC (pop.=4,000,000) and from 1984 to 1997, we found that 614 individuals were AchR Ab positive. In women ages at submission of the first positive sample had a bimodal distribution with peaks at 34 and 54. In men there was a single peak at 65. As this distribution is consistent with previous reports on age of onset, we used the date of submission of the 1st positive sample as an approximation of the date of onset and studied its distribution. We stratified our sample into four age-groups: <19, 19-40, 41-65, >65. and used Pearson correlation coefficient to assess the relationship between date of first positive test and age.

Results: From 1984 to 1997, the proportion of patients>65 has increased in both men and women. The correlation between the proportion of patients over 65 and the year of sampling is significant. ($p < 0.005$ with $r = 0.8$). The proportion of patients >65 increased from 26.8% to 36.9% for men and 18.2% to 23.1% for women. Meanwhile, the proportion of female patients 19 to 40 decreased (p=0.0.003).

Conclusion: The proportion of elderly individuals diagnosed with MG increases over time while onset in women of reproductive age is decreasing. This could be attributed to longer life expectancy, the changing demographics of the elderly, improvement of awareness of MG and its diagnosis criteria, including availability of the test. This trend may have financial implications and needs to be further studied.

D-04

Statin-induced Myotoxicity and Mitochondrial Dysfunction.

N. Sripathi, J.A. Gutierrez, M. Boska (Detroit, Michigan), G.D. Vladutiu (Buffalo, New York).

Background: Mechanism of statin-induced myotoxicity is poorly understood. We describe a group of patients with statin-induced myopathy associated with mitochondrial dysfunction.

Methods: Retrospective analysis of three patients who underwent electrodiagnostic studies (EMG), magnetic resonance spectroscopy (MRS), and muscle biopsy and biochemical analysis.

Results: Case histories: Patient 1: 75-year-old woman with persistent myalgias, proximal weakness and fatigue for five months after lovastatin was discontinued. Patient 2: 54-year-old man developed rhabdomyolysis due to cyclosporin and simvastatin toxicity. He continued to suffer from weakness and myalgias even after discontinuation of simvastatin. Patient 3: 69-year-old woman presented with persistent fatigue and muscle weakness 4 months after discontinuation of simvastatin.

Serum CK activity: 5473(1), 607(2), 366 (3) IU/L. EMG showed denervation and myopathic potentials in all. MRS showed mitochondrial dysfunction (1) and it was normal in the other (3). Muscle biopsy: necrotizing myopathy with ragged red fibers(1), occasional cytochrome oxidase negative fiber (2), increased mitochondrial content in few fibers(3). Biochemical analysis of the muscle: reduced complex II-II, IV activity(2), and markedly reduced esterified carnitine with normal total carnitine(3).

Conclusion: In a subset of patients with statin-induced myopathy, mitochondrial dysfunction may be responsible for persistent symptoms.

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D-05

Familial Myasthenia Gravis: Report of Four Cases Spanning Three Generations and a Review of the Literature

D.J. Sahlas, R.A. Marrie and G. Bray (Montreal, Quebec)

Background: A genetic role for the development of autoimmune myasthenia gravis (MG) is suggested by concordance in monozygotic twins and the increased frequency of other autoimmune diseases in family members of myasthenics. Familial autoimmune MG is rare.

Methods: A patient with a family history of MG was evaluated in hospital. Relatives were interviewed and medical records examined for details regarding the diagnosis of MG in three other family members.

Results: The index case first experienced symptoms of MG at age 75 years. She subsequently developed generalized MG and has required steroids and immunosuppressants to control her disease. Her father developed predominantly bulbar symptoms of MG at age 75 years. His brother developed similar symptoms of MG in his early 60s and died shortly after thymectomy. A 46 year-old nephew of the index case is also beginning to exhibit signs of generalized MG. Acetylcholine receptor antibodies were strongly positive in the index case and her nephew. (The assay was not available for her father and uncle).

Conclusions: Four individuals in three successive generations were diagnosed with autoimmune MG. Study of familial cases such as this may clarify the contribution of genetic factors to the development of this disease.

DEMENTIA

E-01

Is Corticobasal Degeneration Part of the Pick Complex?

A. Kertesz, W. Davidson, D.G. Munoz (London, Ontario), P. Martinez-Lage (Navarra, Spain)

Rebeiz et al. described corticodentronigral degeneration, subsequently renamed corticobasal degeneration (CBD), and recognized similarity of the pathology to Pick's disease (PiD). Subsequent emphasis was on the uniqueness of CBD. Clinical CBD does not always correspond with CBD pathology and it has been described with Pick bodies. Other cases pathologically typical of CBD have frontal lobe dementia (FLD) or primary progressive aphasia (PPA) without extrapyramidal features. In this study we document the close association of the behavioural disorder of FLD and PPA with CBD and the overlap of CBD type of pathology with other varieties of the PiD.

Twelve patients with CBD syndrome all developed progressive aphasia (PA) (7) or FLD (5) as a secondary syndrome and those with FLD had subsequent PA within a few months to a few years. The reverse pattern of PPA, subsequently developing CBD, was also frequent (9). Five FLD cases with purely behavioural presentations later developed CBD as well. The postmortems showed C BD pathology, two Pick bodies and one spongiosis gliosis and neuronal loss only. The results support the hypothesis that FLD, PPA and CBD are significantly overlapped clinically and represent a spectrum that is continuous with PiD.

E-02

Disorientation to Time as a Predictor of Progression to Alzheimer's Disease for Age-Associated Cognitive Decline Patients

L. Verret (Qu bec, Qu bec), H.M. Chertkow, H. Bergman, L. Babins, N. Kelner, V. Whitehead (Montr al, Qu bec)

Background: Age-associated cognitive decline (AACD) individuals have subjective memory complaints, mild memory impairment on objective neuropsychological testing, yet do not fully meet criteria for dementia. About 15% of AACD patients will decline to dementia annually. To date, no marker or test is available to predict progression.

Design/Methods: 90 AACD patients received clinical and neuropsychological evaluation and were followed annually for 3 years. After follow-up, 44 had developed Alzheimer's Disease (AD) (henceforth progressors), and 46 remained AACD (henceforth non-progressors). Retrospective analysis of initial cognitive testing was used to construct a score for temporal orientation modified from Benton's Temporal Orientation Test (BTO)(Benton et al, 1964).

Results: Using a score >1 on the modified BTO as a cut-off point, 16 out of 44 (36.4%) of progressors scored as high probability of progression, and all non-progressors scored as low probability of developing AD. This yielded a specificity of 100% and a positive predictive value of 100%.

Conclusion: Our study suggests that any AACD patient showing a significant degree of temporal disorientation (scored on the modified BTO as >1) on initial or close follow-up evaluation has a 100% chance of meeting diagnosis criteria for AD after 3 years follow-up.

E-03

Cerebrolysin (CL): a Neurotrophic Agent for the Treatment of Alzheimer's Disease (AD)

Panisset M, Gauthier S, (Montr al, Qu bec) and the Cerebrolysin Study Group

Background: Cholinergic neurons are the primary focus of AD pathology and can be salvaged by neurotrophic factors. CL is a porcine brain derived peptide preparation with a known neurotrophic activity on cholinergic neurons.

Goal: to test the efficacy of CL in the treatment of AD.

Method: Multicentre (14 Canadian centres) randomized, double- blind, placebo-controlled, parallel-group study of CL in patients with mild (MMSE 14 to 26) probable AD. After signing informed consent, fulfilling selection criteria and having baseline assessments, subjects received intravenous injections of 30 ml CL diluted in 100 ml normal saline or placebo five days per

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week for four consecutive weeks. Assessments were then made at one, three and six months after baseline.

Results: Data was available on 189 patients. The CL was slightly older than the placebo group (75.19+/-0.64 vs 73.20+/-0.63, p= 0.030). There was a significant difference between the two groups on the CIBIC at three months in favor of CL (76% vs24% with CIBIC score ≤4, p=0.007). This difference was present neither at one nor at six months. This appears to have been caused by a stabilization of the Cerebrolysin group in the face of decline of the placebo group for the first three months. The Cerebrolysin deteriorated to the level of the placebo group at six months. There were no differences in the incidence and the severity of adverse events. No significant adverse events were related to the injections.

Comments: Cerebrolysin appears to have stabilizing properties for two months after the one month treatment phase. This effect is in accordance with the purported mechanism of action of Cerebrolysin. Future protocols should further assess the neuroprotective effect of CL and using sustained administration of the drug.

E-04

Propentofylline for the Treatment of Alzheimer's Disease: A 72-Week Study Assessing Safety, Efficacy, and Impact on Disease Progression

M. Rother (Bridgewater, New Jersey) for the European/ Canadian Propentofylline Study Group

Background: The safety and efficacy of propentofylline, as well as its ability to slow the progression of dementia, were assessed in a multinational, double-blind study of 486 patients with mild-to-moderate Alzheimer's disease (AD).

Methods: During the first 48 weeks (segment I), patients were randomized to propentofylline or placebo. During the final 24 weeks (segment II), half of the propentofylline patients in segment I were switched to placebo and half continued receiving propentofylline. Similarly, half of the placebo patients were switched to propentofylline and half remained on placebo. An effect on disease progression was inferred if the treatment differences achieved during segment I were maintained during segment II.

Results: At the end of segments I and II, global function (CIBIC-Plus) and cognitive performance (ADAS-cog) were significantly improved in propentofylline-treated patients. Withdrawal Analysis: ADAS-cog treatment differences favored propentofylline-to-placebo patients over continuous placebo patients at the end of segment I; these differences were partly maintained in segment II. Similar but less pronounced results were observed for CIBIC-Plus. Delayed-Onset Analysis: After 48 weeks, ADAS-cog and CIBIC-Plus scores favored continuous propentofylline recipients over placebo-to-propentofylline patients; these clinical benefits were only partially diminished at the conclusion of segment II.

Conclusion: Propentofylline provides clinical benefits for AD patients and may slow the progression of dementia. Propentofylline was well tolerated.

Supported by: Hoechst Marion Roussel, Inc.

E-05

Propentofylline for the Treatment of Vascular Dementia: A 48-Week Study Assessing Safety, Efficacy, and Impact on Disease Progression

C. Schweiger (Bridgewater, New Jersey) for the European/Canadian Propentofylline Study Group

Background: The safety and efficacy of propentofylline, as well as its ability to slow the progression of dementia, were assessed in a multinational, double-blind study of 444 patients with probable or possible vascular dementia (VaD).

Methods: During the first 24 weeks (segment I), patients were randomized to propentofylline or placebo. During the final 24 weeks (segment II), half of the propentofylline patients in segment I were switched to placebo and half continued receiving propentofylline. Similarly, half of the placebo patients were switched to propentofylline and half remained on placebo. An effect on disease progression can be inferred if the treatment differences achieved during segment I are maintained during segment II.

Results: At the end of segment I (24 weeks) and up until week 44, global function (CIBIC-Plus) and cognitive performance (ADAS-cog) were significantly improved in propentofylline-treated patients. Withdrawal Analysis: ADAS-cog treatment differences favored propentofylline-to-placebo patients over continuous placebo patients at the end of segment I and were maintained until the end of the study. CIBIC-Plus scores followed a similar trend until week 36. Delayed-Onset Analysis: After 24 weeks, CIBIC-Plus scores favored continuous propentofylline patients over placebo-to-propentofylline patients; these treatment benefits were only partially diminished at the conclusion of segment II. ADAS-cog scores were not supportive of the CIBIC-Plus data.

Conclusion: Propentofylline provides clinical benefits for VaD patients and may slow the progression of dementia. Propentofylline was well tolerated.

Supported by: Hoechst Marion Roussel, Inc.

BASIC NEUROSCIENCES

F-01

Impaired Wallerian Degeneration and Regeneration in Mice Lacking Inducible Nitric Oxide Synthase (iNOS)

D.W. Zochodne, D. Levy, C. Cheng, H. Sun (Calgary, Alberta)

Background: Nitric oxide is released within injured peripheral nerve trunks. We examined the contribution of iNOS expression to axonal degeneration and regeneration in mice with a targeted mutation of the iNOS (inducible nitric oxide synthase) gene.

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Methods: iNOS "knockout" mice (KO) and wild-type (WT) littermates underwent sciatic nerve transection, crush or chronic constriction injury (CCI; a model of neuropathic pain). Wallerian degeneration was studied using quantitative morphometry of intact myelinated fibers (MFs) and fibers undergoing degeneration. Multifiber motor conduction and behavioural measurements of neuropathic pain were correlated with morphometry.

Results: After complete transection, there were delays in the recovery of the M potential from sciatic-tibial reinnervated foot interosseous muscles in KOs 4-10 weeks after injury. Quantitative morphometry identified fewer large caliber MFs, indicating a less mature regenerative stage. At a fixed distance distal to crush at 2 weeks iNOS KOs had fewer regenerating MFs and larger numbers of persistent degenerating fiber profiles than wild-type controls. By 6 weeks, this deficit had recovered. Following CCI with prolonged axonal degeneration, KOs had a delay in MF breakdown, delayed axonal sprouting and a delay in the appearance of neuropathic pain.

Conclusions: The findings indicate that iNOS facilitates axonal breakdown during Wallerian degeneration to permit regeneration.

F-02

Role of Potassium Channels in Axonal Dysfunction After Spinal Cord Injury: Molecular and Electrophysiological Evidence

R. Nashmi, O.T. Jones, M.G. Fehlings (Toronto, Ontario)

Background: The abnormal electrophysiological properties of axons which persist after spinal cord injury (SCI) directly contribute to the neurological deficits and appear to be related to altered K^+ channel expression or activity. However, the specific K^+ channels that mediate axonal dysfunction after SCI has not been established. In this study, we used electrophysiological and molecular techniques to characterize the K^+ channels that may be involved in axonal dysfunction after SCI.

Methods: SCI was performed *in vivo* in rats (23g clip injury for 1 min at T7). Compound action potentials (CAPs) were recorded from chronically injured (6 weeks post SCI) and uninjured dorsal column slices *in vitro* using the sucrose gap technique. Western blots and immunohistochemistry (IMC) were used to examine changes in Kv1.1 and Kv1.2 K^+ channel expression.

Results: Infusion of 4-AP (1 mM) and α-dendrotoxin (α-DTX), which block "fast" K^+ channels, but not CsCl or TEA (which block inward rectifiers and "slow" K^+ channels, respectively) resulted in a significantly greater increase in CAP amplitude of chronically injured as compared to noninjured axons. Following SCI, there was a significant change in the distribution of Kv1.1 and Kv1.2, which encode channels responsive to 4-AP and α-DTX, along axons. Quantitative analysis of Kv1.1 and Kv1.2 expression, as assessed by Western blotting and IMC showed upregulation of expression in white matter along axons.

Conclusions: The changes in expression of Kv1.1 and Kv1.2 after SCI are paralleled by concomitant electrophysiological changes in sensitivity to α-DTX and 4-AP. This work is the first to report a molecular basis for K^+ channel mediated axonal dysfunction after SCI and may facilitate the development of novel molecularly targeted approaches to treat axonal dysfunction associated with chronic CNS injury. *(Supported by MRC Canada, Easter Seal Research Institute, Ontario Neurotrauma Foundation/Rick Hansen Institute).*

F-04

Oligodendroglial Apoptosis Following Spinal Cord Injury: Role in Post-traumatic Axonal Degeneration

Steven Casha, Michael G. Fehlings (Toronto, Ontario)

Introduction: Apoptosis or programmed cell death has been implicated in CNS trauma and ischemia. In this study we used biochemical, molecular and morphological approaches to examine the role of glial apoptosis in axonal degeneration after clip compression spinal cord injury (SCI) at C7-T1 in rats.

Methods: DNA laddering, *in situ* TdT mediated dUTP nick end labeling (TUNEL), and electron microscopy were used to demonstrate apoptosis following SCI. Double labeling with fluorescent labeled cell specific antibodies was performed to identify neurons, glia and microglia. The distribution of the FAS death receptor protein was examined. βAPP immunostaining was used as a marker of degenerating axons.

Results: Apoptotic cells were demonstrated as early as 6 hours following injury, increasing in number over 2 days, and persisting at 2 weeks. Double labeling experiments demonstrated that in this model apoptosis occurs in oligodendrocytes (CNPase +ve) but not neurons (NF200 +ve) or astrocytes (GFAP +ve). TUNEL positive glia were temporally and spatially colocalized with βAPP labeled degenerating axons following injury. FAS immunostaining was demonstrated on oligodendrocytes.

Discussion: These results provide evidence that apoptosis of oligodendroglia occurs after SCI, is associated with axonal degeneration, and may occur through the FAS mediated signaling pathway.

F-05

Neurotrophin Treatment of Injured Retinal Ganglion Cells: the Role of Bcl-2 Proteins

M. Chow, D.B. Clarke (Halifax, Nova Scotia)

Background: In the adult rodent, treatment of injured retinal ganglion cells (RGC) with brain-derived neurotrophic factor (BDNF) has been shown to delay apoptotic RGC death; however, the molecular mechanisms involved remain unclear. The purpose of this study is to determine whether BDNF may exert its RGC survival effect through the regulation of retinal Bcl-2 proteins, including the anti-apoptotic Bcl-x and pro-apoptotic Bax proteins.

Methods: Forty-eight adult female Sprague-Dawley rats

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underwent unilateral intra-orbital optic nerve transection and a 5µl intravitreal injection of (i) BDNF (5 µl; n=4/group), or (ii) 0.1 M phosphate buffered saline (n=4/group). Retinas were examined at 3, 8, 24, 72 hours, 1 week, and 2 weeks by immunohistochemical staining of Bcl-2, Bcl-x and Bax.

Results: The earliest change observed was an increase in the staining of Bcl-2, corresponding to the distribution of Muller cells, in the BDNF-treated retinas at 3 hrs. At 24 hours, Bcl-x staining in BDNF-treated animals was enhanced throughout most of the retina, including the ganglion cell layer.

Conclusions: These results show that neurotrophin treatment of axotomized RGCs has widespread influences on Bcl-2 proteins within the retina and that the mechanism by which BDNF delays apoptosis after optic nerve axotomy may involve the early upregulation of Bcl-2 and Bcl-x.

F-06

Characterization and Expansion of Human Ventral Mesencephalon Cells in Culture

A.O. Hebb, M. Hong, I. Mendez (Halifax, Nova Scotia)

Background: Parkinson's Disease (PD) is a hypokinetic neurological disorder, characterized by the loss of dopamine (DA) neurons of the nigrostriatal pathway. Although transplantation of fetal tissue is currently in clinical trials, the availability of suitable tissue at the time of transplant is limited. To address this limitation, the objective of the present study was to explore the possibility of maintaining hFVM cells in culture as well as the expansion of these cultured cells using the known mitogen, Epidermal Growth Factor (EGF).

Methods: To study the maintenance of hFVM cells in culture, cells were cultured in serum free (SF) media on poly-l-lysine coated plates for 24 hours and 7 days, and then immunostained for Tyrosine Hydroxylase (TH), the rate limiting enzyme in DA biosynthesis. To investigate the expansion potential of hFVM cells in culture, cells were cultured for 7 days in expansion media (EM), and exposed to bromodeoxyuridine (BrdU), a thymidine analog that is incorporated into DNA during DNA synthesis, at five days, and then immunostained for BrdU.

Results: Cultures of hFVM neurons were maintained in culture for 7 days without a decrease in viability, with a TH population of 8.8 ± 2.8 % (S.D.) at 24 hours and 8.8 ± 2.6 % (S.D.) at 7 days. Exposure of EGF treated hFVM cell cultures to BrdU resulted in a mixed population of both BrdUir and non-BrdUir cells.

Conclusions: The results demonstrated that hFVM cells with a stable TH+ population of cells can be maintained in culture for 7 days without decreased viability. Furthermore, when cultured in expansion media, a population of cells are capable of expanding through cell division.

CEREBROVASCULAR SURGERY

G-01

Comparison of Endovascular and Surgical Treatment of Anterior Communicating Artery Aneurysms

P.D. McNeely, E.J.Versnick, R.O. Holness, B. Baxter, W. Maloney, R. Vandorpe (Halifax, Nova Scotia)

Background: Guglielmi Detachable Coil (GDC) embolization and surgical clipping are both accepted treatment modalities for anterior communicating artery aneurysms. It is currently unknown which approach is most effective. The purpose of this study is to compare short term outcomes for both treatment methods.

Methods: A retrospective review of all patients with anterior communicating artery aneurysms who were treated at our centre between January 1995 and November 1998 was performed. We collected data concerning Hunt and Hess (H & H) grade at presentation, length of hospital stay, days in the Intensive Care Unit (ICU), and mortality. We then compared the surgically treated and endovascularly treated groups.

Results: Forty-nine patients were enrolled. Of this group, 15 were treated by GDC embolization and 34 by surgical clipping. The average length of stay for patients with unruptured aneurysms was 12 days for the surgical group, including 4 days in the ICU, and 4 days for the endovascular group, with no time spent in the ICU. For patients with H & H grades 1 and 2, length of hospital stay was 20 days when treated surgically and 13 days when treated endovascularly. Hospital stay for patients presenting with H & H grades 3 to 5 was 32 days for the surgical group, and 20 days for the endovascular group. Both treatment modalities were associated with similar mortality rates.

Conclusions: In our series, endovascular embolization was associated with a reduced length of hospital and ICU stay for patients presenting with asymptomatic aneurysms or with good clinical grade subarachnoid hemorrhage. Further comparative analysis of patients presenting with H & H grades 3 to 5 will be presented.

G-02

Management Outcome of Patients with Unruptured Cerebral Aneurysms Treated at the Kingston General Hospital

F. Espinosa, D. Westergaard, R. Smith(Kingston, Ontario)

Background: The mortality rate after aneurysm rupture varies from 40.7-52.9% The annual incidence of rupture for all previously unruptured aneurysms is approximately 1.4%. Objective: To determine which patient factors and aneurysm characteristics influenced outcome and to evaluate the management of unruptured aneurysms, with emphasis on neurological outcome and the incidence of major surgical complications.

Methods: This retrospective chart review included 71 patients

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with 99 unruptured intracranial aneurysms. Aneurysm size and morphology were determined angiographically. Patients were graded according to the Glasgow Outcome Score 3 months after surgery, or at the last follow-up visit for untreated patients.

Results: Advanced age, female gender, history of hypertension, and aneurysm related symptoms at diagnosis impacted negatively on outcome. Small aneurysm of the anterior circulation were associated with the best outcomes, and aneurysm neck: sac ratio did not influence outcome. Patients treated surgically fared better than those managed conservatively, and 91.3% of surgical patients had a good outcome. Patients treated conservatively had a 46.2% mortality. The surgical complication rate was 39%, with no deaths.

Conclusion: Given the high rates of morbidity and mortality among conservatively managed patients, it is recommended that all patients be offered surgery for the clipping of unruptured aneurysms.

G-03

Surgical Anatomy and Treatment of Paraclinoid Carotid Artery Aneurysms

J. Max Findlay (Edmonton, Alberta)

Objective: The author reviewed the anatomy, surgical treatment and outcome of a series of ICA aneurysms arising near the anterior clinoid process.

Methods and Results: 28 patients with 30 paraclinoid ICA aneurysms have undergone surgery between 1989-1998. 79% were female, 30% presented with SAH, 17% with visual failure, and 53% were found incidentally. 20 aneurysms arose adjacent to the ophthalmic artery and projected in a superior direction relative to the ICA, 9 arose from the inferior surface of the ICA lifting the ICA above the sac, and one aneurysm arose from the upper surface of the ICA distal to the ophthalmic artery. 37% of aneurysms were <10mm in diameter, 50% were 10-24mm, and 4 were >25mm. Cervical ICA suction/aneurysm deflation was used in 10 patients, hypothermic circulatory arrest in 4, deliberate proximal ICA occlusion in 1, and two aneurysms were explored only. Surgical complications included one ICA occlusion (resulting in blindness), two cases of incomplete clipping (one resulting in hemorrhage and death), and two cases of anterior choroidal artery occlusion causing hemiparesis. Overall, there were 20 good outcomes.

Conclusion: After the ICA enters the subarachnoid space it slopes upward in an anteroposterior direction until it curves and becomes more vertical near the origin of the posterior communicating artery. Its paraclinoid port therefore has an inferior (or "ventral") and superior (or "dorsal") surface. The majority of aneurysms in this region arise form the dorsal surface near the ophthalmic artery ("ophthalmic" ICA aneurysms), but another large group, which tends to present as large aneurysms causing visual failure, arise from the ventral surface of the ICA ("ventral" or "superior hypophyseal artery" ICA aneurysms). Liberal removal of the anterior clinoid process and methods to gain proximal ICA control and deflate large and giant ICA aneurysms facilitate surgical clipping and add little risk to the procedure. Clipping strategies will be discussed.

G-04

Preoperative Cerebral Angiography as a Predictor of Carotid Stump Pressure during Endarterectomy

S.P. Lownie, R.A. Larrazabal, M. Eliasziw, G.G. Ferguson, H.W.K. Barr, R. Sahjpaul (London, Ontario)

Background: The purpose of this study was to determine whether preoperative angiographic findings can predict intraoperative stump pressure values and therefore whether they can predict ischemic cerebral events caused by carotid artery cross-clamping during carotid endarterectomy.

Methods: A total of 102 patients who underwent cerebral angiography followed by carotid endarterectomy were included in this study. The angiograms were reviewed for: spontaneous cross-flow into ipsilateral middle cerebral artery (MCA) branches; patency of anterior communicating artery (Acomm), size of the ipsilateral Al, contralateral A1, and ipsilateral posterior communicating (Pcomm) arteries; and degree of ipsilateral and contralateral carotid stenosis. Mean systemic pressure and mean stump pressure were obtained intraoperatively. A multiple regression analysis using backward elimination was performed to select the anatomical features that best predicted stump pressure.

Results: Only systemic pressure, contralateral carotid stenosis, contralateral A1 size, and Acomm filling were found to be significant (p-values of 0.001, 0.002, 0.029, 0.013, respectively). Middle cerebral artery cross-flow, ipsilateral A1 size, and ipsilateral Pcomm were far from being significant. A regression equation was obtained. Stump = 1/3 Systemic - 10 Con Sten + 10 Con Al + 10 Acomm. The results have fair predictive ability (R-squared = 24.4%).

Conclusion: The preoperative angiogram can help to predict stump pressure values and therefore it may help to predict ischemic events caused by carotid cross-clamping during carotid endarterectomy.

G-05

Delayed transmural extrusion of coils from aneurysms following endovascular treatment: a possible mechanism of recurrent aneurysm formation.

G. Pickett, S.P. Lownie (London, Ontario)

Background: The introduction of Guglielmi electrically detachable platinum coils for the endovascular treatment of aneurysms has provided an appealing alternative to craniotomy and clipping. However, recurrence of the aneurysm at its neck and proximal portion has been described following apparent complete occlusion at the time of coiling. One proposed mechanism attributes this to coil compaction due to the ongoing force of arterial pressure. Another mechanism has been that of regrowth and enlargement of the aneurysm at the level of the neck.

Methods and Results: We describe an unusual phenomenon observed in two patients. The first was a 46-year-old man who

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developed a recurrent basilar aneurysm between 5 and 12 months post-coiling. During surgery for definitive clipping, he was found to have bare loops of coil over the dome of the aneurysm, although the bulk of the coil mass remained within the sac. Similarly, a 65-year-old woman developed recurrent filling of a previously coiled left internal carotid bifurcation aneurysm. At surgery, two loops of coil were seen outside of the lumen of the aneurysm. Neither of these patients had any coil penetrating the aneurysm dome during the original coil treatment.

Conclusion: We propose a third possible mechanism for aneurysm recurrence following detachable coil treatment. Gradual extrusion of coil loops through the dome of the aneurysm may occur, allowing more of the aneurysm lumen to fill at follow-up angiography.

GENERAL NEUROLOGY

H-01

Lumbar Spinal Stenosis Masquerading as Polyneuropathy.

D.J. Sahlas, J.D. Stewart and C.H. Chalk (Montreal, Quebec)

Background: The classical presentation of lumbar spinal stenosis (LSS) is neurogenic claudication, possibly with lumbosacral polyradiculopathy. When the latter is prominent, LSS can sometimes be difficult to distinguish from polyneuropathy (PN). We describe four such patients, discuss how these disorders can present similarly, and suggest distinguishing features.

Methods: Four patients were evaluated clinically, underwent electrodiagnostic studies, and were imaged with CT or CT myelogram. Two patients subsequently had laminectomies performed.

Results: The patients presented with back pain, distal leg weakness with sensory impairment, and hypo/areflexia at or below the knees. Claudication and radicular pain were present in two. Nerve conduction studies and electromyography showed abnormalities predominantly in the distal lumbosacral distribution, suggestive of PN. Imaging revealed moderate to severe LSS in each case. Further investigations did not reveal another cause for PN.

Conclusions: LSS can resemble PN when radicular involvement is symmetrical. Furthermore, dorsal root ganglia can be intraforaminal or intraspinal in some patients, and hence subject to root compression resulting in abnormal sensory action potentials (a feature usually distinguishing between polyradiculopathy and PN). Finally, differential (predominantly distal) neurological involvement in LSS might be an axon length phenomenon. These factors explain why LSS can masquerade clinically and electrophysiologically as PN.

H-02

Withdrawn

H-03

Representation of the Visual Field in Human Occipital Cortex: A Magnetic Resonance Imaging and Perimetric Correlation

James A. Sharpe and Agnes M.F. Wong (Toronto, Ontario)

We evaluated the retinotopic map of the human occipital cortex by correlating MRI findings with visual field defects in patients with occipital lobe infarcts. Compatibility between our clinico-neuroimaging findings and locations of lesions predicted by the classic Holmes map was assessed.

Methods: MR images were obtained in 14 patients with occipital lobe infarcts. Visual field analysis was performed with tangent screen, Goldmann perimeter and Humphrey Field Analyzer. Based on the pattern of visual field deficit, the location of lesion in the mesial occipital lobe in each patient was predicted using the Holmes map and other retinotopic maps of occipital cortex. The predicted location of the lesion was compared to its actual location shown on MRI to assess the compatibility between our data and the other maps. These maps determine retinotopic correlates of the medial occipital lobe, but they cannot establish correlates of area V1 (striate) cortex. The medial occipital representation of central vision was evaluated by regression analysis.

Results: The MRI correlations in this study confirmed gross estimates of the retinotopic organisation of the occipital cortex. However, our findings did not correlate exactly with the Holmes map. We determined that the central 15° of vision occupies 37% of the total surface area of the human medial occipital lobe. We present a refined retinotopic map.

Conclusions: The resolution of conventional MRI testifies to its considerable value in localising occipital lobe lesions. Our findings refine the Holmes map of human occipital cortex.

H-04

Quantifying Ocular Torsion in Oculomotor and Combined Oculomotor and Trochlear Nerve Palsies: An Aid to Localization

James A. Sharpe and Mohammed Fouladvand (Toronto, Ontario)

Objective: To measure ocular torsion in the presence of isolated oculomotor and trochlear nerve palsies and combined oculomotor and trochlear nerve palsy, in order to determine violations of Listing's law and to aid in their localization.

Background: Combined third and fourth nerve palsy is seldom recognized, and usually specifies involvement in the cavernous sinus. If vascular in origin, ischemia in the distribution superior branch of the inferolateral trunk of the intracavernous segment of the internal carotid artery is considered responsible. Disturbed incyclotorsion in the presence of a third nerve palsy would then implicate damage in the cavernous sinus. Listing's law constrains torsion in tertiary gaze positions.

Methods: We measured torsion in middle-aged or elderly patients with: 1) Presumed isolated diabetic third nerve palsy; 2)

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Isolated fourth nerve palsy, and 3) Combined third and fourth nerve palsy. We used a 3-dimensional magnetic search coil technique with Fick co-ordinates. We computed ratios of vertical to torsional and horizontal to torsional eye position changes in tertiary gaze positions and determined movement out of Listing's plane.

Results: Combined third and fourth nerve palsy showed low ratios of intorsion to adduction amplitudes (mean 0.25, SD 0.03), but violations of Listing's law were nonetheless evident. Presumed isolated third nerve palsy caused higher ratios of adduction to intorsion (means 1.16, SD 0.52 to 0.94, SD 0.49) and greater departures from Listing's plane. MRI showed no brainstem, intracavernous or other lesions. Combined third and fourth nerve palsies and isolated third nerve palsies resolved within 6 weeks, supporting an ideopathic, presumably ischemic mechanism.

Conclusions: Measuring monocular torsion in the presence of third nerve palsy can detect and quantify concurrent fourth nerve palsy. Identification of associated fourth nerve palsy may obviate MRI or other investigations pending resolution of the palsy because it points to an intracavernous site of nerve damage.

H-05

Geographic and Temporal Distribution of Mortality Rates for Multiple Sclerosis (MS) in Canada, 1965-94.

S. Warren, K. G. Warren, L. Svenson (Edmonton, Alberta)

Background: There have been several studies of MS prevalence rates across the Canadian provinces, but no recent studies of MS mortality.

Methods: Mortality rates for MS in the Canadian provinces from 1965-94 were examined using Statistics Canada data. This agency codes mortality based on the International Classification of Diseases. The numbers represent only those individuals whose death had MS listed as the primary or underlying cause. The data were used to calculate age-adjusted mortality rates/100,00 population for each of the 10 Canadian provinces separately and overall, by 5-year periods starting in 1965 (standardized to the 1991 Canadian census data using the direct method).

Results: In 1990-94, the highest MS mortality rates were in Ontario= 4.9 and Quebec= 4.8. The Western provinces had intermediate rates: British Columbia= 2.3, Alberta= 2.8, Saskatchewan= 2.4, Manitoba= 2.4. The Atlantic provinces had the lowest rates: New Brunswick= 1.0, Nova Scotia= 1.3, Newfoundland= 1.2, Prince Edward Island= 1.5. Overall mortality rates for the ten provinces were 2.4 in 1965-69, 2.5 in 1970-74, 2.1 in 1975-79, 1.6 in 1980-84, 1.8 in 1985-89, and 2.4 in 1990-94. There was a decline in mortality rates during the 1980's, but the rates rose again in the early 1990's. In general, this same pattern was observed within the provinces.

Conclusion: Disparities in MS mortality rates exist among the Canadian provinces, and mortality rates have fluctuated over time.

H-06

Genetic and Reproductive Counselling in MS: Practical Information for Neurologists

A.D. Sadovnick (Vancouver, British Columbia)

Genetic factors are recognized to have important roles in the overall etiology of multiple sclerosis and in the familial aggregation of the disease. Increasingly, patients are asking neurologists about familial risks and reproduction. Familial risk information should be based on the specific pedigree, incorporating the important co-variates of gender, age of MS onset and whether or not one parent has MS. The lifetime prevalence of MS for a Caucasian of northern or central European ancestry is approximately 0.2%. Familial risks can range from approximately 3% (one affected first-degree relative) to approximately 22% (sister of female MS patient who had an early disease onset and a father with MS) to approximately 40% (monozygotic co-twin). As MS is a disease which often affects individuals during the child bearing years, genetic counselling often includes reproductive counselling. In addition to family risk data, reproductive counselling includes discussion of: teratogenicity, pregnancy outcome, effect of pregnancy and delivery on maternal MS, and longterm prognosis. As more MS therapies are approved, potential teratogenicity is a major concern to both patients and physicians.

H-07

Direct Intracranial Pressure Monitoring in the Posterior Fossa: A Clinical Study.

P. K. Narotam (Winnipeg, Manitoba), P. Govender and S. S. Nadvi (Durban, South Africa)

Introduction: The perceived risks of cerebrospinal fluid leakage, brain stem irritation, cranial nerve damage and infection have restricted posterior fossa ICP monitoring (pICPM). Forty-one patients underwent pICPM following surgery for a variety of neurosurgical conditions: tumors (24), trauma (9), hypertensive hemorrhage (4), sepsis (3) and AVM (1). In 11 patients (dual monitors) concomitant supratentorial ICPM was performed.

Results: A rise in ICP occurred in 9 patients. The mean peak ICP was 31.3mmHg (range=16-48) which occurred at a mean time of 6.7 hours (range 1-12). The CT-Scan features of raised pICP ("tight posterior fossa") were effacement/compression/displacement of the 4th ventricle, compression of the perimesencephalic & pontine cisterns, absence of the quadrigeminal cisterns and obliteration of CSF around the cerebellar sulci. Of 11 patients with dual ICPmonitors, 5 had bi-compartment lesions. The compartment with the expanding pathology exhibited high ICP first except for hydrocephalus (synchronous).

Conclusions: The rise in pICP occurs earlier and more rapidly in the posterior fossa. Differential ICPs depend on the "compartment" in which the lesion expands and on the patency of CSF pathways. This is the largest series demonstrating the safety and value of direct pICPM as an early indicator of

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potentially remediable complications, especially in trauma & spontaneous hemorrhage.

H-08

Development and Introduction of a Formal Evidence Based Medicine Curriculum in a Neurology Training Programme.

S. Wiebe, B. Demaerschalk, M. Jenkins (London, Ontario)

Background: Evidence Based Medicine (EBM) teaching/practice vary widely in amount, depth and structure among Canadian neurological training programmes. No formal educational EBM neurological curricula exist. Having assessed the perceived need, relevance, and acceptability of EBM in neurological training, we developed and implemented a formal EBM neurology curriculum at the University of Western Ontario.

Method: The structure adheres to adult learning theory, emphasizing self-directed, interactive, self-evaluative tutorials, and shunning passive information transfer. Curriculum contents follow the Royal College of Physicians and Surgeons' recommendations. Specific topics contributed by all teaching neurologists and trainees, rated by relevance, were organized by specialty. EBM topics include informatics, clinical epidemiology, biostatistics, and economics. Trainees' time constraints determined the frequency/duration of tutorials.

Results: Twice-monthly, 1.5-hour tutorials of distilled theme-modules cover the 5-year residency. The curriculum is recursive and flexible. EBM principles are emphasized at the beginning of each academic year and reviewed in all tutorials, which revolve around a specific clinical case. Summarized evidence and clinical application are captured in edited, 2-page, pocket-size, critically appraised topics.

Conclusions: One year (25 tutorials) after its implementation, the curriculum is integral to the residency programme. Formal curricula are feasible and effective vehicles to incorporate EBM teaching in neurological training.

GENERAL NEUROSURGERY

I-01

Persistent Pain following Lumbar Spinal Surgery in 1000 Patients

E. Berger, (Montreal, Quebec)

The intent of this study is to investigate the relationship between post-op chronic pain, objective neuro-muscular findings and subjective pain perception. A series of 600 patients with single operations and 400 with multiple operations were examined clinically and radiologically 51 and 38 months respectively following surgical intervention in work related accidents. In the group of 600 patients perineural fibrosis was diagnosed pre-op in 0.67% and post-op in 11%. In the group of 400 patients with multiple operations, at the time of the second operation, the incidence of perineural fibrosis had risen to 47%. In the 600 patient group with single operations 17.17% considered themselves improved, 31.67% unchanged and 51.33% thought -themselves worse than pre-op. 22.84% in the same group complained of chronic post-op lumbar pain only while 59.32% complained of lumbar and unilateral leg pain and the remaining 17.83%, of lumbar and bilateral leg pain. Four years after operation only one quarter of the patients had returned to some kind of remunerative work

Conclusion: In order to achieve better post operative results proper patient selection and techniques to avoid perineural fibrosis are of paramount importance.

I-02

Anterior Reconstruction of Symptomatic Anterior Cervical Pseudarthrosis

P. Chan (Calgary, Alberta), M. Hadley (Birmingham, Alabama)

Background: Pseudarthrosis is an uncommon complication following anterior cervical discectomy and fusion (ACDF). Pseudarthrosis after ACDF is often symptomatic and may require treatment.

Methods: We performed anterior cervical revision using autologous iliac crest graft, with or without plating, in 49 consecutive patients with symptomatic pseudarthrosis following ACDF. The mean age of the 49 patients was 42.5 years. Forty-one patients (84%) had pseudarthrosis at one level, and 8 (16%) at 2 levels. The indications for reoperation of pseudarthrosis were intractable neck pain, with or without radiculopathy/myelopathy, in the presence of non-union on plain cervical spine x-rays.

Results: The average follow-up period was 23.9 months. Solid bony fusion was achieved in 56 out of 57 levels (98%) treated in all 49 patients. Forty-five of the 49 patients (92%) exhibited good to excellent outcome in terms of radiculopathy/myelopathy and neck pain, while 4 patients were rated fair to poor despite solid fusion. Twenty-nine of the 35 patients (83%) who were employed prior to reoperation were able to return to work. No major complications were encountered in our series.

Conclusions: We conclude that anterior reconstruction using autologous iliac crest bone graft, with or without plating, is effective and safe in treating symptomatic anterior cervical pseudarthrosis following ACDF.

I-03

A Prospective Randomized Double-Blind Controlled Trial to Evaluate the Efficacy of an Analgesic Epidural Paste Following Lumbar Decompressive Surgery

R.J. Hurlbert, N. Theodore, J.B. Drabier, A.M. Magwood, V.K.H. Sonntag. (Calgary, Alberta)

Background: Pain control can often be improved by local (as opposed to systemic) application of analgesics and/or anaesthet-

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ics. The purpose of this study was to evaluate a single dose epidural analgesic "paste" in the control of post-operative pain following lumbar decompressive surgery.

Methods: Sixty patients undergoing routine elective lumbar decompressive surgery were randomized in a double blind fashion to one of two groups: active versus placebo paste. The paste was applied to the exposed dura at the time of surgery, just prior to wound closure. Patients were followed in-hospital and at home for 3 months after surgery. Several outcome measures were studied to look for differences in pain control and to ensure comparability between groups.

Results: Patients receiving active paste demonstrated significantly lower pain scores compared to those receiving placebo paste for up to 6 weeks post-operatively. General health perception indexed by the SF-36 was also significantly better in patients receiving paste for up to 6 weeks. In-hospital and outpatient oral narcotic consumption was significantly lower in the actively treated group. Inpatient straight leg testing was improved in active compared to control patients.

Conclusions: Administration of an analgesic paste directly to the epidural space during lumbar decompressive surgery significantly improves post-operative pain control, reduces prescribed analgesic consumption, and improves overall health perception for up to 6 weeks following surgery. We conclude that this post-operative pain control strategy is both effective and safe, and may provide a new standard of pain management in patients undergoing lumbar discectomy or laminectomy.

I-04

Endovascular Management of Giant Distal Cerebral Aneurysms

I.B. Ross (Winnipeg, Manitoba), J. Moret, A. Weill, M. Piotin (Paris, France)

Background: The management of giant aneurysms (GAs), which often requires parent vessel occlusion (PVO), is difficult when there are limited pathways for collateral flow. We aimed to determine the outcome from endovascular treatment of GAs located downstream from the Circle of Willis.

Methods: 24 patients, with 24 GAs, were evaluated for possible endovascular treatment. Eight aneurysms were selectively embolized and 8 were treated with primary PVO, with or without distal vascular bypass. Eight patients could not be treated endovascularly.

Results: Selective aneurysm embolization resulted in no anatomical cures. Two patients died of SAH in the follow-up period. One coiled patient, who went on to subsequent spontaneous PVO, and all 8 patients treated primarily with parent vessel occlusion, were considered cured by their treatment. Only 2 PVO patients had periprocedural ischemia, none of which resulted in a permanent problem. Of the eight that could not be treated endovascularly, one succumbed to surgery, four died while being followed conservatively, and three could not be located for follow-up.

Conclusions: Selective aneurysmal coiling is usually not curative in this situation, though it may provide some protection from subsequent bleeding. In selected patients, PVO is a safe and effective. Simple observation is not recommended.

I-05

Anterior Cervical Fixation with a Load Sharing System: One Year Follow-up of 110 Cases.

T. Kaibara, R.J. Hurlbert, (Calgary, Alberta)

Background: Neurosurgery has experienced the incorporation of instrumentation into anterior procedures for cervical decompression and fusion. Current titanium plating systems provide several advantages over earlier systems, including load sharing mechanics, which may improve bony fusion. Experience with over 100 cases using a locking titanium plating system is presented.

Methods: Since 1996, anterior cervical decompression and reconstruction augmented with a load sharing plate system has been performed in 110 patients. The titanium anterior locking plates were applied under fluoroscopic guidance and supported post-operatively with rigid external orthoses. Clinical and radiographic assessments were performed at regular intervals to evaluate bony fusion.

Results: Procedures were performed for trauma (n=59), degenerative disease (n=47), neoplasia (3) and infection (n=1). Radiographically at 12 months percent change in superior screw angle was 0.1% ± 2.8 (s.d.), percent change in inferior screw angle was 2.3% ± 7.2, and graft subsidence 1.4% ± 3.5. Radiographic fusion was observed in all patients at 12 months. No plate failures occurred, however a single case of screw breakage was noted.

Conclusions: Our experience with over 100 cases suggests that load sharing internal fixation may provide improved rates of cervical fusion.

I-06

Minimally Invasive Laminectomy

B.H. Guiot (Ottawa, Ontario) R.G. Fessler (Gainesville, Florida)

Background: Lumbar laminectomy can significantly relieve neural compression, but is often associated with major tissue disruption relating to the exposure. Minimally invasive techniques may be useful in these situations to reduce the extent of tissue trauma, which in turn may temper the post-operative stress response that is known to result in unfortunate complications following otherwise uneventful procedures. The purpose of this study is to determine the feasibility of endoscopically decompressing the lumbar spine.

Methods: In this cadaver study, unilateral microendoscopic laminotomy, bilateral microendoscopic laminotomy, unilateral open laminotomy and bilateral open laminotomy were performed in the lumbar spine. Each procedure was performed at

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every level from L1 to L4 in four cadavers. Pre and post laminotomy CT scans were obtained to assess decompression of the spinal canal.

Results: The above procedures were successfully performed at every level. Decompression of the spinal canal and neural structures was achieved regardless of the approach used. A unilateral endoscopic approach proved as effective in achieving decompression but was less disruptive to the soft tissue structures than the other methods. Complications, including dural tears and facet complex instability were independent of the procedure performed.

Conclusion: Minimally invasive techniques can be used to decompress the spinal canal. They may prove to be beneficial in decreasing complications related to the surgical stress response.

I-07

Rationale, Indications and Timing of Decompressive Surgery for Spinal Cord Injury: Evidence-based Meta-analysis

Michael G. Fehlings, Charles Tator. (Toronto, Ontario)

An evidence-based meta-analysis of the experimental and clinical literature was conducted to evaluate critically the rationale, indications and timing of decompressive surgery for the treatment of acute, nonpenetrating spinal cord injury (SCI). Evidence from clinical trials was categorized as Class I (well-conducted randomized prospective trials), Class II (well-designed comparative clinical studies), or Class III (retrospective studies). Studies in animal models of SCI consistently demonstrate a beneficial effect of early surgical decompression, although it is difficult to apply these data directly to the clinical setting. Clinical studies provide suggestive (Class III and limited Class II) evidence that decompressive procedures improve neurological recovery after SCI. However, no clear consensus can be inferred from the literature as to the optimum timing of decompressive surgery. Many authors have advocated delayed treatment to avoid medical complications, although there is good evidence from recent Class II trials that early decompressive surgery can be performed safely without added morbidity or mortality. In conclusion, there is biological evidence from experimental studies in animals that early surgical decompression may improve neurological recovery after SCI, although the relevant interventional timing in humans remains unclear. Decompressive surgery for SCI can only be considered a practice option. Analysis of the literature does not allow definite conclusions to be drawn regarding appropriate timing of intervention. There is a need for well-designed experimental and clinical studies of the timing and neurological results of surgical decompression for the treatment of acute SCI.

I-08

Continuous Intrathecal Opioid Treatment in Chronic Pain of Nonmalignant Etiology: Long Term Effects and Efficacy

Krishna Kumar, Mike Kelly, T. Pirlot (Regina, Saskatchewan)

Background: The therapeutic concept of administration of opioids into the cerebrospinal fluid is the result of studies concerning the discovery and localization of specific binding sites. The unique feature of spinal opioid analgesic is pain control without production of sensory or motor deficiencies.

Method: In the last four years we have implanted fourteen patients for treatment of chronic pain with programmable Synchromed pump (Medtronic) for drug delivery intrathecally, the drug most commonly utilized being morphine. Clonidine or fentanyl have also been used alone or occasionally in combination with morphine. The follow-up period was 3.3 years to 5 months (mean 1.6 years).

Results: Deafferentation pain and nociceptive pain showed the best long term results, with 75% and 43% pain reduction (visual analog scale), respectively. The mean morphine dosage initially administered was 1.11 mg/day (range 0.2 - 6.5 mg/day); after 6 months it was 3.1 mg/day (range 0.4 - 8.75 mg/day). In a long term observation of 5 patients who received intrathecal morphine for longer than 2 years, no patient had a constant dosage history and all 5 patients (100%) showed an increase in morphine dosage up to 10 mg/day 1 year after dosage determination. Eight patients (57%) were satisfied with the therapy and ten patients (72%) reported improvement in their quality of life. One patient developed tolerance requiring use of drug combination and in two cases the pumps were explanted due to intolerable side effects. One case required revision due to pump malfunction and one patient needed revision of the intrathecal catheter due to disconnection. Side effects such as constipation, disturbed micturition, pruritus, nausea, cold sweats were observed initially but improved with time.

Conclusion: Intrathecal opioid for treatment of nonmalignant pain is valuable method in selected group of patients.

I-09

Growth Hormone Response in Children with Growth Hormone Deficiency Following Cranial Irradiation For Brain Tumors

R.F. Del Maestro and C.L. Clarson, (London, Ontario)

Background: Growth hormone deficiency is frequent in children receiving cranial irradiation therapy for the treatment of brain tumor. This study was carried out to evaluate growth in response to growth hormone therapy in children with growth hormone deficiency (GHD) due to cranial irradiation for a primary brain tumor.

Method: Height velocity in response to growth hormone therapy was assessed in 40 children with GHD. In 18 the GHD was due to cranial irradiation for brain tumor and idiopathic GHD was present in 22.

Results: Children in the brain tumor group were significantly taller at diagnosis compared to the idiopathic GHD group (height standard deviation score: -2.1 ± 0.9 v - 3.6 ± 1.0 $p < .001$). Height velocity in the year prior to diagnosis was not significantly different in the two groups, 3.2 ± 0.9 for GHD secondary to irradiation and 3.3 ± 1.0 cm/yr for the idiopathic GHD. However, height velocity was significantly greater in the first two years after the initiation of growth hormone therapy in the

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idiopathic group when compared to the brain tumor group (Yr. 1: 10.8 ± 2.6 v 18.7 ± 1.6, p < .005; Yr. 2: 8.6 ± 1.9 v. 6.6 ± 1.6, p < .005).

Conclusions: Earlier detection of GHD following cranial irradiation for brain tumor may explain the increased height of children diagnosed with GHD in this group. Since children in the brain tumor GHD group have decreased response to growth hormone therapy early recognition and treatment of GHD is crucial to optimize final height.

I-010

Hemifacial Spasm Natural History and Treatment

A.M. Kaufmann, R. Ranawaya, T. Lye, G. Olsen (Calgary, Alberta)

Background: Repeated botulinum toxin (Botox) injections provide good temporary relief of hemifacial spasm (HFS) symptoms, while excellent long-term control or cure may be achieved with microvascular decompression (MVD) surgery. We report our local experience in the management of patients with HFS.

Methods: We reviewed the charts of all 54 HFS patients treated with Botox in a single clinic (RR). The extent of HFS was objectively defined by the number of regions injected with Botox at each visit (e.g. frontal, periorbital, cheek, perioral, platysma). Telephone questionnaires were also completed to provide subjective assessment of HFS severity and satisfaction with treatments.

Results: Ages ranged from 23-93 years, duration of HFS 1-23 years and Botox injections were repeated for 0.3-17 years, with an average number of 2.8 injections/year/patient. One patient had bilateral disease.

The extent of HFS increased in 74% (23/31) of patients having > 60 month disease history. Time since onset was 8.1 years for the 55% having increased extent, and 4.6 years in the 45% with no increased extent (p<0.05).

Sixteen patients underwent MVD surgery between November 1997 and December 1998. The extent of preoperative Botox injections had increased in 11 and not increased in 5, although severity of spasms had increased in all. Post-operatively, 88% had no further spasms and 12% had partial (>75%) reduction of spasms. None had hearing loss or new facial weakness. These patients were among the consecutive surgical series of 136 MVD procedures (AMK) with 0% stroke/death rate and <1% risk of ipsilateral deafness.

Conclusion: HFS typically begins periorbitally, and Botox injections may provide good initial relief. However, the extent and severity of disease can be expected to increase, and Botox control of lower facial spasms is generally unsatisfactory. Therefore, patients with HFS should be offered MVD by specialized surgeons having established records of effectiveness and safety in performing this surgery.

I-011

Microvascular Compression Findings in Trigeminal Neuralgia

A.M. Kaufmann, T. Lye, G. Olsen (Calgary, Alberta)

Background: Microvascular compression (MVC) of the trigeminal nerve root entry is the widely accepted cause for most cases of idiopathic trigeminal neuralgia (TN). However, an association between the nature and extent of MVC and outcome following therapeutic interventions has not been well established. We report an analysis of intra-operatively observed MVC and outcome following microvascular decompression (MVD) for TN.

Methods: In a consecutive series of 59 MVD procedures for typical TN performed by the senior author, details of MVC were prospectively recorded. Outcome was determined by telephone questionnaires completed by a research assistant blinded to MVC scores. Outcome definitions were: excellent = 98% pain reduction & no medication; good = >75% pain reduction & occasional medications; fail = <75% pain reduction & chronic medications. Minimum patient follow-up was 10 months.

Results: MVC upon the symptomatic trigeminal nerve was identified and decompressed in all patients. The most prominent compression in each case was: large artery in 71% (e.g. superior cerebellar artery); large vein in 22%; and small unnamed vessel in 7%. Nerve indentation/distortion was observed in 51% versus simple nerve contact by the vessel in 49%.

Surgical outcome was excellent/good in 88% (78% & 10%), including 90% with large artery, 92% with large vein, but only 25% with isolated small vessel MVC. MVD of large vessels (artery or vein) was associated with excellent/good outcome compared to isolated small vessels (91% versus 11%; p=0.001). However, there was no association with nerve indentation/distortion and favorable outcome compared to simple nerve-vessel contact (93% versus 79%, p=0.19)

Conclusion: MVD is an effective treatment of TN, especially when MVC is due to large arteries like the superior cerebellar artery or large veins. For MVD to be successful, it is not necessary that the offending vessels mechanically indent or distort the nerve. Therefore, all vessels contacting the nerve should be mobilized and decompressed in order to optimize results of MVD for TN.

STROKE

J-01

Thrombolytic Treatment in Acute Stroke: The Calgary Experience

P.A. Barber, N. Newcommon, J. Zhang, H. Karbalai, A.M. Buchan (Calgary, Alberta)

Background: The NIH /NINDS and ECASS (I and II) trials have established the efficacy of tissue plasminogen activator (tPA) in acute ischaemic stroke. The practical challenge is to

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provide an effective stroke care delivery system so that patients can be appropriately selected for interventional treatment.

Method: In total 68 consecutive patients have received intravenous tPA at a dose of 0.9mg/kg within 3 hrs of ischaemic stroke symptom onset. Baseline neurological deficit was measured using the National Institute of Health Stroke Score (NIHSS) and outcome was measured using the modified Rankin Score (mRS). The CT scans were scored at baseline and at 24 hrs using the Alberta Stroke Program Early CT (ASPECT) Scoring System.

Results: Of the 65 patients treated, 11 violated the established protocol. The mean NIHSS in the intent to treat group was 14 (S.D 5.36). Functional outcome, was categorized into independent (mRS 0,1,2), dependent (mRS 3,4,5) and dead (6). A favorable outcome was seen in 37 patients (65 %[95% CI 53- 77]) and 6 patients (10 %[95% CI 2.5-18]) died. Protocol violations had a significant impact on the overall treated mortality (Pearson Chi Square P =0.004) and there was an increased risk of symptomatic intracerebral hemorrhage (Fisher Exact P=0.05). The risk of poor outcome (mRS3,4,5, or 6) decreased as the ASPECT score increased (Pearson chi-square test p=0.001). An ASPECT score of 7 or less increased the risk of poor outcome (Pearson Chi-Square P<0.0001). In addition a score of 7 or less is strongly predictive of a poor outcome (mRS 3,4,5 or dead) showing a predictive positive value of 100%, a predictive negative value of 77%, a sensitivity and specificity of 38% and 100% respectively.

Conclusions: We believe tPA treatment for acute stroke is transferable from the setting of a randomized controlled trial into a community environment and that tPA can be effective. The use of the ASPECTS score is a feasible method of quantifying injury on CT scans, and suggests the possibility of identifying subgroups of patients who are at increased risk, or who have a higher probability of benefiting, from this therapy.

J-02

Delayed Intracranial Hemorrhage as a Complication of Angioplasty and Stenting of Extracranial Carotid Stenosis.

A. Douen, W. Morrish, S. Grahovac, P. Kalapos, R. Wee, M. Richard, C. Agbi, N. Pageau, L. Pratt, S. Mandino (Ottawa, Ontario)

Background: Carotid endartectomy can significantly reduce the risk of stroke in symptomatic patients with severe carotid stenosis. Carotid angioplasty and stenting has been advocated as a possible alternative to carotid endarterectomy.

Methods: Thirty one patients with severe carotid stenosis, considered poor surgical candidates by neurology and neurosurgery, were offered angioplasty and stenting using Wallstents. A total of 40 vessels were stented (mean stenosis = 84.5); 34 internal carotid arteries (ICA), 4 common carotid arteries (CCA), and 2 external carotid arteries. Thirty nine procedures were successful.

Results: Three patients who had uncomplicated, unilateral ICA stent procedures and were completely well in the immediate post-operative period developed intracranial hemorrhages at 0.4, 2.5 and 6 days post stenting. ICA stenosis in these patients were 90, 90 and 95%, respectively. Patients were not hypertensive during or following the procedure. The 2 earliest hemorrhages were large, fatal intraparenchymal bleeds. The third patient presented with seizures and had a focal non-fatal hemorrhage in the right frontal lobe.

Conclusions: Delayed intraparenchymal hemorrhage, likely representing cerebral hyperperfusion injury, can occur following stenting of carotid arteries. A similar phenomenon has been reported following carotid endartectomy; incidence 0.4%. The higher incidence of hemorrhage observed here (7%; 3 of 38 ICA/CCA vessels) may reflect our small study population. In addition, patient selection, severity of stenosis and preexisting medical conditions may be mitigating factors.

J-03

Importance of Cardiac Akinetic Segments in Cerebral Embolism

Z. Nadareishvili, Z. Choudary, C. Joyner, D. Brodie, J.W. Norris (Toronto, Ontario)

Background: There are various causes for ischemic stroke complicating acute myocardial infarction (AMI), including cardiac arrhythmias, left ventricular dysfunction and mural thrombosis.

Methods and Results: We investigated 83 patients during the first week in a coronary care unit for the presence of cerebral microembolism (high intensity transient signals-HITS) using transcranial doppler (TCD). All patients had echocardiograms. 94% of patients were anticoagulated and 39% received thrombolytic therapy. We detected HITS in 16% of patients and found a higher prevalence in anterior infarcts (22%) compared to inferior lesions (8%), and HITS were seen in 2 of 3 patients with mural thrombosis. Abnormal wall motion was significantly associated with HITS ($p < 0.01$). The incidence of mural thrombosis was lower than most series possibly due to the use of anticoagulant and thrombolytic agents, but in these patients HITS appeared to be more frequent.

Conclusions: HITS are persistent in spite of anticoagulant and thrombolytic therapy in AMI with cardiac akinetic segment and may be an underestimated cause of cerebral embolism.

J-04

Is Most Extracranial Arterial Dissection Traumatic?

Z. Nadareishvili (Toronto, Ontario), J.W. Norris (Toronto, Ontario) for the Canadian Stroke Consortium

Background: With the increasing safety of neurovascular imaging, dissection of the extracranial arteries is becoming a more frequent cause of ischemic stroke especially in young patients.

Methods and Results: A prospective study is being undertaken by the Canadian Stroke Consortium. Preliminary data on 12

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patients (3 males and 9 females) indicates that neck manipulation is a major cause (7/12) and occurs within 1-2 days of the procedure. All seven patients were females, mean age 41 ± 10 years, and all experienced neck pain at the time of the manipulation. One patient died, two made uneventful recovery but the remainder were permanently disabled. A history of trauma was only made in some patients by careful retrospective history-taking, suggesting that in many cases the cause could be missed.

Conclusions: Neck manipulation is an important cause of ischemic stroke in young people and the traumatic etiology may frequently be overlooked.

J-05

The Utility of Echocardiography in the Diagnosis and Management of Cardioembolic Stroke

C. Jaigobin, K. Bernard, M. Kapral, F. Silver (Toronto, Ontario)

Objective: To identify the number of patients with ischemic stroke in which the results of echocardiography (ECHO) produced a diagnosis of cardioembolic stroke (CES) and a change in management.

Methods: We conducted a retrospective analysis of 289 consecutive patients admitted to the Toronto Hospital Stroke Unit between January 1, 1996 and June 30, 1997. Patients were assessed with electrocardiogram (EKG), CT or MRI, carotid dopplers and ECHO. During this period, 207 patients were investigated with ECHO. All 207 patients were examined with transthoracic echocardiography (TTE) and 11 with additional transesophageal echocardiography (TEE). Chart review was conducted for each patient and an etiological diagnosis was reached at each of the following three stages: clinical assessment at admission with CT and EKG, after all investigations except ECHO and, after ECHO.

Results: A final diagnosis of CES was reached in 100 patients. This was made at admission in 46 patients (40 with atrial fibrillation, 3 with acute MI, 2 with mechanical valves and 1 with cardiomyopathy. The remaining 54 patients had a diagnosis of CES after ECHO (48 after TTE and 6 after TEE). The following abnormalities were identified by TTE: left ventricular hypokinetic or akinetic segments (22), mitral annular calcification (20), rheumatic changes on mitral valves (2), left ventricular aneurysm (2), patent foramen ovale (1) and left atrial mass (1). TEE identified the following abnormalities: patent foramen ovale (3), hypokinetic left ventricular segment (1), mitral valve (1) and aortic valve (1) mass lesions. There were direct management changes in 8 patients.

Conclusions: ECHO is an important tool in the assessment and management of patients with ischemic stroke. Both TTE and TEE enable identification of cardiac abnormalities not apparent by routine clinical assessment and EKG.

J-06

A High Regional Rate of Surgery for Asymptomatic Carotid Artery Stenosis?

J. Max Findlay, John H. Wong, Tracey Lubkey, Donna Boyd (Edmonton, Alberta)

Background: We have been auditing the indications and results of CEA's in Edmonton since 1994, and in this update examine the performance of CEA for asymptomatic carotid stenosis over this period.

Methods: All patients undergoing CEA in our city (where all CEAs in Northern Alberta are performed) since April 1994 have been reviewed for demographic information, operative indications and surgical results. Preoperative cerebral angiograms were reviewed by an investigator blinded to patient identity and reported degree of stenosis. Clinical follow-up to 30 days was carried out by a medical-outcomes specialist. The results of interim analyses of the audit, along with clinical practice guidelines (emphasizing surgery for asymptomatic stenosis as "uncertain"), have been circulated to the medical community and CEA surgeons in our region.

Results: The rates of CEA and post operative stroke and/or death within 30 days of surgery for asymptomatic stenosis was 40% and 5.1% of 291 operations between April 1994 and September 1996, 40% and 2.7% of 184 operations between September 1996 and September 1997, and 45% and 2.7% of 249 operations between October 1997 and October 1998.

Conclusion: A high rate of surgery for asymptomatic carotid artery stenosis persists in our city, especially in comparison to a progressively smaller rate of surgery for symptomatic moderate (50-69%) stenoses (22%, 11% and 8% of all CEAs for the 3 audit periods). Asymptomatic carotid artery stenosis is a common problem that continues to be a popular indication for surgery in our community. Fortunately the major surgical complication rate in this group of patients has fallen.

J-07

Familial Cerebral Aneurysms and Arteriovenous Malformations: Inherited Cerebral Vasculopathy?

R. Leblanc, (Montreal, Quebec)

Introduction: Patients with a cerebral arteriovenous malformation (AVM) can have coexistent cerebral aneurysms. This may result from hemodynamic stresses when the aneurysms are within the nidus of the AVM or on a major feeding artery but aneurysms also occur on arteries not submitted to the hemodynamic effects of the AVM Thus aneurysms and AVMs may result from a more widespread cerebral vasculopathy than is currently appreciated. Support for this concept would be gained by identifying families in whom both conditions exist. We report three such families.

Methods & Observations: We have encountered 3 families in whom different individuals harboured either a cerebral aneurysm or an AVM. An informant provided details of the family history and the presence of the lesions was confirmed angiographically and/or histologically in all cases. Family 1. A 24-year-old woman

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developed hemiplegia from the rupture of a parasagittal AVM. A maternal cousin, a 31-year-old female, died in the post-partum phase from a ruptured posterior communicating artery aneurysm. She also had an ophthalmic artery aneurysm. Family 2. A 38-year-old man had a tectal hemorrhage from the rupture of a small AVM. He had a 15-year-old nephew who died from the rupture of an intracranial vertebral artery aneurysm. Family 3. A 33-year-old woman had chronic headaches associated with a parasagittal AVM. She had a 50-year-old sister who sustained a cerebral hemorrhage from a ruptured middle cerebral artery aneurysm.

Conclusions: The well recognized occurrence of cerebral aneurysms and AVMs in the same patient and the presence of aneurysms or AVMs in different individuals of the same family as reported here suggest that these conditions, at least in some individuals, may reflect a cerebral vasculopathy that can express either aneurysms, AVMs, or both lesions. This may result from alterations in the molecular signaling system involved in cerebral vasculogenesis and/or later angiogenesis. The phenotypic lesion produced (aneurysm, AVM, and perhaps other vascular malformations such as cavernous angiomas and capillary telangiectasias) would depend on the time when the molecular alteration occurs and on the pathway affected.

J-08

The Occurrence and Treatment of Cerebral Venous Thrombosis in a Tertiary Care Centre

T. Jeerakathil, A. Shuaib (Edmonton, Alberta)

Background: Cerebral venous thrombosis (CVT) is a condition involving thrombosis of the dural sinuses. The condition may have an extremely variable presentation and prognosis. Common treatment options include ASA, heparin and warfarin. Endovascular thrombolysis is another therapy that is being offered and has shown some promise in case reports. We investigated the University of Alberta experience in regards to the number of cases identified and the treatments utilized over the past ten years.

Methods: A retrospective chart review was conducted with patients followed up by telephone. Patients with a diagnosis of non-septic thrombosis of the cerebral venous sinuses were included. Neonatal cerebral venous thrombosis was not included in the review.

Results: A total of eighteen charts have been identified so far. Clinical presentation was noted to be quite variable ranging from headache and mild numbness to seizures and coma. Heparin, followed by warfarin was the most common treatment given. A small number of patients received ASA alone. Three out of eighteen patients died. The majority of patients went on to a good recovery with minimal neurological disability. More details in regards to neurological morbidity and outcome will be presented.

Conclusions: Although it is difficult to make definitive conclusions based on a retrospective review, cerebral venous thrombosis is a relatively uncommon disorder at our institution. CVT resulted in approximately eighteen admissions to our tertiary care centre over a period of ten years. Prognosis is generally good but death and significant neurological morbidity can result. Most neurologists elect to treat with intravenous heparin followed by warfarin.

J-09

Long Term Cognitive Effects of Prosthetic Heart Valves

Z. Nadareishvili, S. Black, S. Fremes, D. Kurzman, M.Freedman, L. Leach, J.W. Norris (Toronto, Ontario)

Background: Acute neurological complications of prosthetic heart valves (PHV) are well established, and infrequent (2-3%) but the long term effects, especially on cognition, remain unknown.

Methods and Results: We are evaluating the neurological and neuropsychological effects of PHV, including evaluation of high intensity transient signals (HITS) using transcranial doppler. In 23 patients (15 mechanical and 8 tissue PHV) in which there were 11 aortic, 9 mitral and 3 with both, 5 became symptomatic over three month to three years follow up: one with vascular dementia, two with TIAs and two with stroke. HITS counts did not differ significantly between symptomatic and asymptomatic patients, or aortic and mitral valves, but were significantly ($p < 0.05$) more frequent in patients with mechanical than tissue PHV and in dual positioned valves. Neuropsychological data on 18 of these patients evaluated by Pearson correlations and ANOVAs indicated that there is no significant correlation between the HITS count and a computerized measure of normal neuropsychological function (memory, attention, language).

Conclusions: Mechanical PHV and dual valve replacement are significant source of cerebral microembolism, but so far this relates only indirectly to neurological and neuropsychological changes.

J-10

Endovascular Treatment of Direct Carotid Cavernous Fistula:

A. Alkhani, R. Willinsky, K. TerBrugge, W. Montanera. (Toronto, Ontario)

Background: Direct high flow (type A) Carotid Cavernous Fistula (CCF) may complicate head injury, ruptured intracavernous carotid artery aneurysm or systemic vascular diseases. Since its introduction in the mid-seventies, endovascular treatment of CCF developed rapidly to become the treatment of choice.

Method: A retrospective data base, chart and films review of thirty two patients with direct CCF managed at The Toronto Hospital between 1984-1998 was carried out. Twenty nine CCF had interventional treatment. Detachable balloons were used alone in 17 cases (59%) , or combined with trans-arterial detachable coils and Glue in 3 cases (10%) or with trans-venous detachable coils in 5 cases (17%). Two cases were treated with

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trans-arterial glue or coils only, and two cases required surgical intervention.

Results: Three patients had spontaneous resolution of their CCF. Out of the 29 patients treated with interventional technique, successful treatment was achieved in 89% of the treated cases. The internal carotid artery was preserved in 57% of the cases. One mortality and four morbidities occurred.

Conclusions: Endovascular techniques are successful in the treatment of CCF. Excellent results may require more than one approach. The ongoing improvement in the used tools and experiences promise better outcome and fewer complications.

NEURO-ONCOLOGY

K-01

Median Length of Stay of 1 or 0 Day Respectively for Patients Undergoing Awake Craniotomy or Stereotactic Biopsy for Intra-axial Brain Tumour

Mark Bernstein, Michael Taylor (Toronto, Ontario)

Introduction: Awake craniotomy (AC) with brain mapping and image-guidance, and frame-based stereotactic biopsy (SB) are two appropriate options for the surgical management of the majority of patients with supratentorial intra-axial tumours, resulting in low complication rate and minimal resource utilization.

Methods: A prospective trial was undertaken of 644 patients with intra-axial supratentorial tumors (approximately 2/3 gliomas and 1/3 metastases) operated under local anesthetic by a single neurosurgeon from 1991 until December, 1998. There were 255 AC and 389 SB. During the same time period 128 craniotomies for intra-axial tumor were performed under general anesthesia because of patient language barrier, aphasia, or cognitive impairment, or awkward location of the tumour. Extra-axial tumours were excluded from this series.

Results: Significant complications were seen in 3.9% of AC and 2.6% of SB patients. Since October 1996, 55 SB and 16 AC patients have been discharged home the same day as surgery, 2-6 hours after surgery. The median LOS of the remaining AC patients since 1996 is 1 day. As patients were not assigned to different treatment groups on a randomized basis, statistical differences between groups would be meaningless and are therefore not presented.

Discussion and Conclusions: Awake craniotomy is an excellent alternative to craniotomy under general anesthesia for most intra-axial tumours requiring resection as it allows for brain mapping, has a low medical and neurological complication rate, and results in decreased resource utilization. A selected number of AC and essentially all SB can safely be performed as Day Surgery cases.

K-02

Familial Gliomas

V. Balasingam, R. Leblanc, (Montreal, Quebec)

Introduction: Gliomas are known to cluster within well-defined, genetically-determined conditions, such as Turcot and Li-Fraumeni syndromes. The occurrence of gliomas within families without other recognizable syndromes is being increasingly recognized. Reports to date, however, have been restricted to brief case presentations without systematic analysis.

Materials & Methods: We report the familial clustering of gliomas in the absence of other recognized syndromes in 3 new families and analyze these and 77 other reported families for pertinent epidemiological and biological features.

Results: 204 individuals from 80 families had a glioma. There were 132 males and 72 females (male/female ratio: 1.8/1; for GBM: 2.1/1). The age at presentation ranged from 0.3-81 years (mean 41.3 years). The histology was specified in 198 cases: glioblastoma multiforme (GBM): 107, anaplastic astrocytoma: 36, low grade astrocytoma: 31, oligo-dendroglioma: 13, and mixed oligo-astrocytoma: 11. Individuals within the same family had the identical type of tumour in 69% of cases (i.e.: GBM and GBM), and the tumour was of the same cell line in another 22% (i.e.: GBM and astrocytoma). The relationship of involved individuals was specified in 108 cases: brother-brother: 29, brother-sister: 21, father-son: 10, sister-sister: 9, mother-sister: 8, father-daughter: 7, mother-daughter: 5, other: 19. In 50% of families symptoms occurred within the same decade and in 62% affected individuals were of the same sex.

Discussion: Recent advances in molecular neurobiology have identified the underlying etiology of some familial brain tumour syndromes traditionally grouped as phacomatoses as well as other familial cancer syndromes. Our observations that first degree relatives are predominately affected by familial gliomas, the predominance of males and the histological concordance of the tumours suggest that there is a distinct, putatively genetically-determined syndrome accounting for clustering of gliomas within families in the absence of other commonly recognized conditions. This hypothesis is testable by current techniques of molecular neurobiology.

K-03

The Dynamics of Malignant Cerebral Tumor Invasion: A Dance in Three Dimensions

R.F. Del Maestro, R.Shivers, W. McDonald, A. Ranger and J. Megyesi (London, Ontario)

Background: The invasiveness of malignant cerebral tumor cells is a dynamic process requiring the degradation of the extracellular matrix and complex cell-matrix, cell-cell interactions. We have developed a time-lapse videomicroscopy system to elucidate the dynamic mechanisms underlying the invasive paradigm of malignant cerebral cells in three-dimensional culture.

Methods: Spheroids and cell aggregates from C6 astrocytoma

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and human medulloblastoma cell lines were implanted into collagen type I gels (Vitrogen 100) and cell invasion monitored. Scanning and transmission EM were used to assess the matrix architecture and the static components of cell invasion. Time-lapse videomicroscopy was used to monitor the dynamic components of cell movement.

Results: The collagen type I matrix is a complex three-dimensional milieu which individual tumor cells degrade to invade. Videomicroscopy outlined at least two invasive paradigms used by cells. In Type I the invading cells extend a single invadopodia that makes a solid interaction with the matrix. The cell body then moves very suddenly in the direction of the anchored invadopodia. This movement is characteristic for C6 astrocytoma. In Type II numerous invadopodia are extended and retracted and movement of the major cell mass is slow. Cell-cell interacting occur when one cell's invadopodia contacts another cell body resulting in immediate retraction of the invadopodia and movement in another direction. This very complex movement is seen in Daoy medulloblastoma cell aggregates.

Conclusions: Malignant cerebral cell movement through three- dimensional gels may be characterized as a complex interactive cell dance having multiple cell-matrix and cell-cell dynamic components. Different cell types use different cell movement paradigms to accomplish invasion and this may have important therapeutic implications.

K-04

Expression and Hypoxic Regulation of Angiopoietins, A Novel Angiogenic Molecule, and its Receptors in Human Astrocytoma Cell Lines and Tumor Specimens:

A. Guha, H. Ding, A. Nagy (Toronto, Ontario)

Introduction: Tumor angiogenesis, whereby new blood vessels are induced from pre-existing vessels are critical for the growth of solid tumors. Vascular Endothelial Growth Factor (VEGF) is a major inducer of tumor angiogenesis and edema in malignant human astrocytomas, by its induction and activation of cognate endothelial specific receptors (flt1; flk1/Kdr). Tie1 and Tie2/Tek are novel endothelial specific receptors, with Angiopoietin1 & 2 (Ang1&2) being ligands for the latter. These angiogenic factors and receptors are crucial for the maturation of the vascular system, but their role in tumor angiogenesis, especially astrocytomas, are unknown.

Methods/Results: Northern blot analysis on human astrocytoma cells demonstrate that Ang1 is expressed by some lines, which in contrast to VEGF, is downregulated by hypoxia. Northern analysis on operative specimens demonstrate Ang1 expression only in low grade astrocytomas, while malignant astrocytomas express both VEGF and Ang2. Cellular localization for expression of Angiopoietins and their cognate receptors with in-situ hybridization and immunohistochemistry, are currently being undertaken on varying astrocytoma grade specimens. Whether the reciprocal regulation of VEGF and Angiopoietins by hypoxia, as noted by the cell culture experiments, are observed around hypoxic zones in the astrocytoma specimens is of special interest.

Discussion/Conclusions: From our initial data, we suggest an interplay between VEGF and Angiopoietins in regulating tumor angiogenesis in human astrocytomas. Low grade astrocytomas are associated with increased Ang1 expression compared to normal brain. Conversion to malignant grades is associated with loss of Ang1, increased Ang2 (a natural antagonist of Ang1), and increased VEGF expression. The biological mechanism(s) of these observations on tumor angiogenesis in astrocytomas will be discussed.

K-05

Astrocytomas are Growth-Inhibited by Farnesyl Transferase Inhibitors Through a Combination of Anti-Proliferative and Anti-Angiogenic Activities.

A. Guha, M.M. Feldkamp, N. Lau (Toronto, Ontario)

Introduction: While 25% of human cancers express oncogenic Ras mutations, such mutations are not found in astrocytomas. We have previously demonstrated that overexpression of the Platelet-Derived and Epidermal Growth Factor receptors in astrocytomas results in functional upregulation of the Ras pathway.

Methods/Results: Six astrocytoma cell lines (U87, U138, U343, U373, U118, and U118:$p140^{EGF\text{-}R}$) were evaluated for their sensitivity to growth-inhibition by the farnesyl transferase inhibitors (FTIs) L-739,749 and L-744,832. All cell lines demonstrated high levels of activated Ras•GTP, despite the absence of oncogenic Ras mutations. All cell lines were growth-inhibited by L-744,832, with the LD_{50} for L-744,832 ranging from 5.3 μM (U138) to 17.4 μM (U343). U118 cells transfected to express the truncated constitutively phosphorylated EGF receptor ($p140^{EGF\text{-}R}$) common in high-grade astrocytomas demonstrated increased sensitivity to both agents.

Discussion/Conclusions: In this paper we demonstrate that FTIs exert their anti-proliferative effect in astrocytomas through a combination of anti-mitogenic and anti-angiogenic effects. Both agents reduced activity in the mitogenic Ras-Raf-MAPK signaling pathway. In addition, both agents reduced the secretion of the potent and specific angiogenic factor Vascular Endothelial Growth Factor (VEGF). In particular, both agents blocked the hypoxic induction of VEGF (mRNA and protein) seen under hypoxic conditions. The combination of anti-mitogenic and anti-proliferative effects suggests that these agents may possess an even greater anti-tumorigenic role *in vivo*.

K-06

Photodynamic Therapy of Malignant Brain Tumors: Results from a Phase 2 Trial and Demographics from a Phase 3 Trial.

Paul Muller, Brain Wilson, Lothar Lilge (Toronto, Ontario), Michael Hitchcock, Fred Hetzel, Qun Chen (Denver, Colorado), Robert Fenstermaker (Buffalo, New York), Robert Selker (Pittsburgh. Pennsylvania)

Photodynamic therapy [PDT] is a local treatment for malig-

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nant tumors. In a phase 2 trial in patients with supratentorial gliomas treated at St. Michael's Hospital, Toronto, and the Swedish Medical Center, Denver, with 2mg/kg Photofin i.v. and intraoperative cavitary PDT, we were able to conclude that PDT was safe in patients with either newly diagnosed or recurrent supratentorial malignant gliomas. There appears to be prolongation of survival in selected patients when an adequate light dose is used. The surgical mortality rate was less than 3%. The combined serious mortality-morbidity rate was <8%.

We have initiated randomized prospective trials to determine if the addition of PDT to standard therapy [surgery, radiation and/or chemotherapy] prolongs the survival of patients with newly diagnosed malignant astrocytic tumors and whether high light dose PDT [120 J/cm2] is superior to low light dose PDT [40 J/cm2] in patients with recurrent malignant astrocytic tumors. Entry criteria include a Karnofsky score ≥70 and age ≥18. The pathology need be glioblastoma or malignant astrocytoma [astrocytoma grade 3 or 4 as defined by the Daumas-Duport classification]. The tumor must be judged suitable for radical resection on the basis of imaging studies.

Thirty-two patients have been randomized in the two studies. There were 18 males and 14 females with an age range of 19-76. Seventeen are recurrent and 15 are newly diagnosed. Twenty-seven are White, 4 Asian and 1 Black. The perioperative mortality- morbidity rate is less than in the phase 2 trial.

K-07

Intratumoral Chemotherapy with Bleomycin for Cystic Craniopharyngiomas in Children

W.J. Hader Jr., P. Steinbok, J. Hukin, C. Fryer (Vancouver, British Columbia)

Background: Surgical removal of cystic craniopharyngiomas is associated with significant morbidity. The purpose of this study was to review our experience with a less invasive therapy, namely, intracystic bleomycin, in the treatment of predominately cystic craniopharyngiomas.

Methods: All children with craniopharyngiomas treated at a tertiary care pediatric neurosurgical centre since 1994, when bleomycin was first used, were reviewed retrospectively. Patients with significant cystic components were considered for cyst catheter placement and intracystic bleomycin as initial therapy. Patients received 2-5mg bleomycin per dose, 3 times per week, for 3-5 weeks as an initial course.

Results: 14 patients, 11 newly diagnosed tumors and 3 with tumor recurrences, were included in the study. Seven patients with new cystic lesions and one with a cystic recurrence underwent insertion of a cyst catheter and partial decompression. Seven patients received intracystic bleomycin therapy. Mean follow up in these patients was 2.5 years. In five patients, treatment resulted in stabilization or decrease in tumor size. Two patients progressed and underwent resection, and one patient had surgical removal because of persistent headaches, although no growth of residual tumor had been noted. Complications related to intracystic bleomycin included hemorrhage into the tumor cyst in 2 patients and peritumoral edema in one patient.

Conclusions: Intracystic bleomycin is a useful, relatively safe therapy for cystic craniopharyngiomas, and may control tumor growth and delay potentially harmful resection and/or radiotherapy in young children.

K-08

Invasiveness of Medulloblastoma Cells in Collagen Gels: Characterization and Response to Surgery and Radiation

A. Ranger, W. McDonald, E. Moore and R.F. Del Maestro. (London, Ontario)

Background: The survival of medulloblastoma patients continues to be limited by local recurrence and leptomeningeal dissemination. This is linked to the inability of our present modalities of therapy to control the invasive subpopulations of residual tumors at the tumor resection site. These studies were carried out to 1) quantify the invasiveness of medulloblastoma cell lines in a three-dimensional model, 2) outline the mechanism of invasion and 3) assess the impact of surgical excision and radiation on invading cells.

Methods: Tumor cell aggregates were made from 5 human medulloblastoma cell lines (Daoy, UW 228-1, UW 228-2, UW 228-3 and Madsen) and implanted into collagen type 1 gels and invasion monitored over 5 days. Specific protease inhibitors and proteolytic assays were used to elucidate invasive mechanisms. Surgical excision of the central mass was carried out and the invasion of residual cells monitored. Single dose (0-25 Gy) and fractioned doses of (0-24 Gy) of radiation were used and their influence of invasiveness quantified.

Results: Invasive behavior was not significantly correlated to cell doubling times which ranged from 28-60 hours. Individual cells detached from the cell aggregates in four cell lines, invaded the gels for up to 1200 um and at rates of 50-300um/day. Metalloprotease inhibition resulted in a dose-dependent decrease in invasion. Tumor mass excision although tending to decrease the invasiveness of residual cells did not significantly reduce it. Radiation therapy decreased medulloblastoma invasiveness in a dose-dependent manner.

Conclusions: The invasive activity seen in medulloblastoma cell lines seems to be metalloprotease dependent and influenced little by surgical excision or radiation therapy. New modalities of treatment are needed to modulate medulloblastoma invasive activity.

K-09

CD40 / CD154 Expression in Human Gliomas: A New Pathway for Immunogene Therapy?

I.F. Parney, C. O'Kelly, E. Solano, A. Gainer, C. Hao, K.C. Petruk (Edmonton, Alberta)

Introduction: CD40 binding by CD154 activates professional antigen presenting cells. This pathway is potentially exploitable for

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glioma immunogene therapy. To explore this further, we examined CD40 / CD154 expression and gene transfer in human gliomas.

Methods: Six human glioma cell lines were examined for CD40 and CD154 expression by flow cytometry and reverse-transcriptase PCR. Ten frozen human glioma sections underwent immunohistochemical staining for CD40 and CD154. CD154 genes were transferred to human glioma cell lines by biolistic and retroviral vectors.

Results: Two of six human glioma cell lines expressed CD40 and 0/6 expressed CD154 by flow cytometry. These results were replicated by rtPCR for CD40, but 4/6 glioma cell lines expressed measurable CD154 mRNA. No frozen glioma sections (0/10) had CD40 or CD154 staining. CD154 expression was seen by immunofluorescent staining in human glioma cell lines after both retroviral and biolistic CD154 gene transfer.

Conclusions: Some human glioma cell lines express CD40 but not CD154 protein. Human gliomas do not appear to express either in vivo. CD154 genes can be effectively transferred to human glioma cells with retroviral or biolistic vectors. CD154 gene transfer is a potentially feasible form of glioma immunogene therapy.

K-10

Particle-mediated (Biolistic) Transfection of Glioma and Melanoma Cell Lines: A Preliminary Study in the Preparation of a Cancer Vaccine.

A. Gainer, A. Young, I. Parney, J. Elliott, K. Petruk (Edmonton, Alberta)

Due to their dismal prognoses, glioblastomas and refractory melanomas are prime targets for immunogene therapy. To date, most studies (including our own) have utilized retroviral vectors to achieve transfection. We investigated particle-mediated gene transfer (the gene gun, or biolistics) to transfect two glioma cell lines (U251 and D54MG), and two melanoma cell lines (SK mel 28 and Ed 141). We initially determined transfection efficiency using β-galactosidase as a reporter gene. Next, we measured the levels of IL-12 secreted by biolistically-transfected cells. Finally, we determined levels of IL-12 expression after the cells had been exposed to 20,000 rads of gamma irradiation (an essential step in the preparation of a cancer vaccine). In all groups of the study, n=12.

The mean proportion of cells that expressed the reporter gene, -galactosidase, was 35% and 37% for U251 and D54MG, respectively. For SK mel 28, the mean percentage of cells that expressed β-galactosidase was 40 %. The mean was 57% for Ed 141 cells. Mean IL-12 secretion was 94 pg/10^6 cells/24 h and 1174 pg/10^6 cells/24 h for U251 and D54MG, respectively. The melanoma cultures showed higher mean levels of IL-12 secretion; 1323 pg/10^6 cells/24 h and 1355 pg/10^6 cells/24 h for SK mel 28 and Ed 141, respectively. Finally, after exposure to 20,000 rads of gamma irradiation, mean IL-12 levels were 87, 1205, 2305 and 2238 pg/10^6 cells/24 h for U251, D54MG, SK mel 28 and Ed 141, respectively. These values were similar to, or higher than those of their non-irradiated counterparts.

We conclude that biolistics provides a rapid, reproducible and efficient method to transfect glioma and melanoma cell cultures. Further, exposure to 20,000 rads of gamma radiation does not adversely affect secretion of IL-12 from biolistically-transfected cells. Both the time required for preparation of autologous cancer vaccines and for safety-testing of vaccines would be considerably reduced through the use of particle-mediated gene transfer, a factor which is critical in aggressive cancers which recur within a matter of months.

K-11

The concurrence of Multiple Sclerosis and Central Nervous System Tumors: A Clinicopathologic Review of Seven Patients.

J. Bakker, N. Hagen, P. Forsyth, P. vandenElzen, C. Wallace, L. Metz. (Calgary, Alberta)

Background: While central nervous system (CNS) tumors and Multiple Sclerosis (MS) can be debilitating, their concurrence complicates management strategies and raises questions about their pathogenesis.

Purpose: The purpose of this study is to describe the concurrence of MS in CNS tumor patients and to outline challenges related to diagnosis and management.

Methods: Population based case series.

Results: Of 1,236 CNS tumor patients encountered in an eleven year period at a regional cancer facility, seven were identified as having MS, a concurrence rate several times the expected rate. The diagnosis of MS was made before or at the same time the CNS tumor was discovered in 6 of 7 patients. Patients who received radiotherapy tolerated it and their MS appeared to neither worsen nor improve. A full neurological history, physical examination and neuroimaging were critical to help distinguish progression of symptoms due to tumor from progressive MS.

Conclusions: The concurrence of MS and CNS tumors appears to be more common than expected in a population based survey of CNS tumor patients and therefore clinicians who care for brain tumor patients should have a heightened suspicion of MS. In this cohort, having MS did not alter the overall oncologic management strategy but more careful patient follow up was needed. These preliminary results suggest that MS may predispose to CNS neoplasms or that there may be pathologic processes in common between the two conditions in some patients.

CHILD NEUROLOGY

L-01

Systematic Review of the Effect of Therapeutic Dietary Supplements and Drugs on Cognitive Function in Subjects with Down Syndrome

M.S. Salman (Toronto, Ontario) S. Logan and L. Jones (London, England)

Background: Down Syndrome is the most frequent autosomal

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trisomy and the commonest identifiable cause of learning disability. Various drugs, vitamins and minerals have been widely claimed to increase IQ in subjects with Down Syndrome. This study was undertaken to evaluate these claims.

Methods: Systematic review of randomized controlled trials of dietary supplements and/or drugs reporting any assessment of cognitive function in people with Down Syndrome that were available by December 1996.

Results: Ten trials were identified including 351 participants. None of the trials revealed a cognitive enhancing effect in subjects with Down Syndrome. A meta-analysis was not conducted due to the heterogeneous nature of the population, interventions and outcome measures used. Overall, we have found the quality of the trials to be poor with small number of subjects with few having used adequate method of allocation concealment of the various treatments used.

Conclusions: This comprehensive systematic review provides no positive evidence from the trials analysed that any combination of drugs, vitamins and mineral enhance either cognitive function or psycho-motor development in people with Down Syndrome. Unfortunately because of the small number of subjects involved and the overall unsatisfactory quality of the trials, an effect can not be excluded at this point. At present there is no justification for the use of such regimes outside the context of large well designed trials.

L-02

Outcome of Developmentally Normal Children Presenting in Status Epilepticus

C. Barnard, E. Wirrell (Saskatoon, Saskatchewan)

Objective: To determine predictors of abnormal neurodevelopmental outcome and refractory epilepsy in developmentally normal children presenting with their initial episode of status epilepticus (SE).

Methods: All neurodevelopmentally normal children presenting in SE between 01/87 and 12/96 were identified through the medical records data base at the Royal University Hospital. Demographic data, prior seizure history and details of SE including etiology, duration, type, neurological exam findings, investigations and treatment were obtained by hospital chart review. Information on subsequent seizures and developmental progress after SE was obtained by review of neurology clinic charts and where possible, follow-up interview.

Results: Twenty children with previously normal development presented in SE during this period. 3 (15%) died during the acute hospitalization (1-metabolic disorder, 2-brain tumours) and 17 (85%) survived. Mean follow-up of survivors was 36 months (range 1-176). At follow-up, 11/17 (65%) were developmentally normal while 6 (35%) were delayed. Predictors of developmental delay included age ≤12 months at SE ($p<0.04$), non-idiopathic or non-febrile etiology ($p<0.02$) and abnormal CT scan ($p<0.003$). 10/17 (59%) had no history of seizures before SE. Of these, 2 (20%) developed epilepsy but neither case was refractory. Of the 7 with seizures prior to SE, 1 had refractory epilepsy prior to SE and 2 more developed refractory epilepsy in the follow-up period.

Conclusions: Developmentally normal children presenting in SE have a benign outcome if they are >12 mos of age, have an idiopathic or febrile etiology and a normal CT scan. Most do not develop refractory epilepsy.

L-03

Vigabatrin and the Developing Brain

S.S. Seshia, M. Qiao, K.L. Malisza, M.R. Del Bigio, P. Kozlowski, J.N. Kanfer, U.I. Tuor (Winnipeg, Manitoba)

Background: Vigabatrin (VGB) is now the preferred treatment for infantile spasms (IS). Potentially irreversible changes occur in the brains of immature rats after 5 days(d) of treatment with VGB at doses suggested for children (Sidhu et al 1997).

Methods: Magnetic resonance imaging (MRI), neuropathology and myelin associated enzymes were done on treatment and after discontinuation. Rats were treated with VGB (N=12; 25-40 mg/kg/d) or saline (N=12) from12-26d of age to mimic age/period of treatment for IS. Half were sacrificed at 26d and half at 40d.

Results: Differences between treated and control groups were: (i) At 26d, significant qualitative and quantitative MRI abnormalities in corpus callosum, int. capsule and hypothalamus of treated animals; at 40d, abnormal T2 persisted in the hypothalamus, (ii) At 26d, degenerating axons, dying glial cells and decreased myelin immunoreactivity, myelin basic protein (MBP) and enzymes in the treated group ($P<0.05$); no significant differences at 40d except in MBP content.

Conclusion: The neuropathological changes at 26 days and the persistent abnormalities at 40 days (2 wks after stopping treatment) may have short and long term consequences for brain function. The CNS effect of VGB in young children needs critical study.

Funded by: CHF

L-04

Increased Intracranial Pressure or A Genetic Anomaly?

L. Jad, H. Darwish, V. Lange, A. Ells, W. Astle (Calgary, Alberta)

Background: Pseudopapilledema (PPE) may be difficult to distinguish on ophthalmoscopic appearances from Papilledema (PE). In the absence of retinal hemorrhages, or drusen, children with headaches may be subjected to costly neuroimaging studies and invasive intracranial monitoring in a quest for tumors or pseudotumor cerebri.

Objective: (1) To demonstrate that PPE without drusen occurs in children and their parents. (2) Analysis of fundus photographs may provide clues to the clinician.

Method: Case series study of 3 children and 6 immediate family members. Fundus photographs were reviewed for disc

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size, morphology, hyperemia, blurring and vessels.

Results: 2 boys and 1 girl were identified to have blurred disc margins. Both the girl's mother and grandmother had thickened elevated optic discs. Ultrasonography excluded deep lying drusen. The mother of one boy and the father of the other boy had appearances of PPE. Disc margin, elevation and/or blurring was homogenous. There was no venous engorgement but the vessels seemed to spill over on to the retina. Extreme tortuosity of vessels was seen in one family.

Discussion: PPE without drusen appears to be an autosomal dominant condition. It is suggested there is neuroglial overgrowth to account for the pronounced homogenous disc margin swelling seen in these families. Examination of the parents, and provision of fundus photographs to the patient are necessary steps in the management.

Conclusion: When PE is considered, both parents eyes must be examined to exclude autosomal dominant PPE.

L-05

Rhythmical Leg Movements of Infancy Mimicking Infantile Spasms

D. B. Sinclair (Edmonton, Alberta)

Introduction: A number of paroxysmal events in childhood may mimic seizures. Infantile spasms is a seizure disorder often seen with developmental regression, hysparrhythmia and a poor prognosis (West Syndrome). I describe a group of infants with rhythmical limb movements which mimic infantile spasms.

Methods: Seven infants, 1 male and 6 females with suspected infantile spasms admitted to the Comprehensive Epilepsy Program at the University of Alberta between 1992 and 1998 are reviewed. All patients had long term video EEG monitoring with several events recorded. In addition, basic blood work and a metabolic screen, a neurological and developmental assessment and neuroimaging were performed. The patients were periodically reassessed following discharge.

Results: The age of presentation ranged from 4 months to 10 months (mean 8 months.) All patients had rhythmical limb movements, in clusters, associated with a normal EEG during the events. The movements appear to be voluntary, pleasurable, and both state and position dependent. The events could be voluntarily suppressed and altered by external stimuli. Illustrative case histories and videotapes will be presented. All the children had a good outcome with eventual disappearance of the events. No patient went on to develop seizures or neurological problems.

Conclusion: Rhythmical Leg Movements of Infancy is a form of rhythmical limb movement which may mimic infantile spasms. It appears to be a transient tic disorder or form of self-stimulation of infancy which is benign and self limited. These events do not require extensive investigation or treatment and are associated with a uniformly good outcome. It is important for physicians to recognize this condition in order to avoid unnecessary investigation and treatment and to alleviate parental concern.

L-06

Infantile Colic is a Migraine Related Phenomenon

M.M.S. Jan and A.R. Al-Buhairi (Jeddah, Kingdom of Saudi Arabia)

Background: The clinical features of infantile migraine are difficult to recognize. Infantile colic is a common cause of pain and crying in apparently healthy infants. We hypothesize that infantile colic could represent a migraine related phenomenon. The objectives of this study were to examine this possible relationship.

Method: A series of children diagnosed with migraine headaches were included prospectively. A structured questionnaire was conducted to identify personal and family history of infantile colic. The same questionnaire was conducted on an age and sex matched control group.

Results: 29 children with migraine (72% without aura and 28% with aura) and 29 controls were included. The two groups were very similar in age, sex, education, and socioeconomic status. Children with migraine were 4 times more likely to have history of infantile colic when compared to the controls (95% CI 1.1-15, p=0.02), Family history of infantile colic in the first degree relatives was also more likely in the migraine group (12/29 vs 4/29, p=0.03). When the group with history of infantile colic was examined (n=21), family history of migraine was more likely present as compared to those without infantile colic (18/21 vs 10/37, p=0.0001).

Conclusions: Infantile colic is highly associated with childhood migraine. The excessive crying could be related to headaches or represent an abdominal migraine variant.

L-07

IVIG In The Treatment Of Juvenile Myasthenia Gravis

H. Kolski, J. Boyd, L. MacMillan, J. Vajsar (Toronto, Ontario)

Background: Intravenous immune globulin (IVIG) has been used for the treatment of myasthenia gravis (MG) since 1984. There are few reports evaluating the role of IVIG in children, which is the goal of this series.

Methods: All 6 patients demonstrated a convincing improvement with IVIG administration. Five children required treatment for an acute deterioration in bulbar and/or respiratory status despite aggressive medical management. One patient with mild generalized MG underwent IVIG treatment in preparation for thymectomy. One child received 2 serial IVIG treatments for 2 discrete episodes of myasthenic crisis, 41 days apart.

Results: In 4 patients with moderate-severe bulbar dysfunction, complete resolution occurred within 2-5 days of initiation of IVIG. Two patients (3 episodes of respiratory failure) were intubated +/- ventilated for 0, 9 and 11 days prior to IVIG administration though could be extubated within 4, 2 and 1 days post treatment.

There were no serious complications with IVIG treatment. One patient was treated with IVIG and plasma exchange (PLEX)

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on separate occasions. She responded to both treatments though PLEX was complicated by insertion of a central venous line, pain, hypotension and difficulties with mestinon titration.

Conclusions: IVIG appears to safely accelerate recovery in juvenile MG exacerbations, particularly with respect to respiratory status, and may be used for pre-thymectomy stabilization. It is simpler to administer than PLEX.

L-08

Longterm Outcome of Hydrocephalus Management in Myelomeningocele

S. Tuli, J.M. Drake, M. Lamberti-Pasculli (Toronto, Ontario)

Background: The cerebrospinal fluid (CSF) shunt remains an important ongoing management problem in myelomeningocele (MMC) patients. We reviewed the long term shunt treatment outcome in a prospectively followed group of MMC patients from a single institution.

Methods: Patients prospectively entered into a hydrocephalus data base with a diagnosis of MMC from the years 1987-1996 were selected. All data was verified from the medical records and additional details about the shunt surgery was collected. The outcome of shunt failure was categorized as shunt obstruction, shunt infection, presence of loculated ventricles, overdrainage and other. All deaths were recorded and every attempt to determine causation carried out. Univariate analysis for shunt failure risk factors was accomplished using Log rank statistics and the Kaplan-Meier method of estimation was used to define survivorship. Multivariable analysis was performed for each repeated failure level using a conditional Cox regression model.

Results: 120 (64%) of 189 MMC patients experienced a first shunt failure with a median time of 303 days: 29 (24%) were due to shunt infection. 61 patients experienced a second shunt failure, 38 a third shunt failure and 36 had four or more. Multivariate analysis of risk factors failed to demonstrate any clear risk factors for either first or subsequent shunt failure. Fifteen patients died, 11 from either shunt or Chiari 1 complications.

Conclusions: Shunt complications remain an important cause of morbidity and mortality in MMC patients, particularly shunt infection.

L-09

Stroke in Term Newborns: Clinical Presentation and Long-Term Outcome

C. Sreenan, R. Bhargara, C.M.T. Robertson (Edmonton, Alberta)

Background: Neonatologists frequently counsel a poor prognosis following neonatal stroke. There has been a 3-fold increase in neonatal stroke in this region in 1998 over the yearly average of the previous 15 years. This review summarizes the long-term neurodevelopmental outcome of cranial computed tomography (CT) documented cerebral infarction in a historical cohort of term neonates.

Method: From 1983 through 1997 all surviving neonates from 2 level III Neonatal Intensive Care Units were prospectively identified and assessed at the Neonatal and Infant Follow-up Clinic, Glenrose Rehabilitation Hospital. Retrospective chart review and blinded re-reading of CT scans identified clinical presentation and outcome.

Results: 40 children (mean gestational age 39.7 ± 1.3 w, birthweight 3261 ± 509 g) were followed for a mean of 37.6 (range 12-164) months. A single vascular infarcted area (not multiple) occurred in 65% of neonates, seizures in 90%, and abnormal discharge neurologic examination in 50%. No sequelae were found in 33% of survivors. Sequelae occurred in 50% of children with right-sided lesions (n=10), 69% of those with bilateral lesions (n=16), and 89% of those with left-sided lesions (n=14). Disabilities include cerebral palsy, 18 (45%); mental index <70, 16 (40%); vision loss, 12 (30%); and epilepsy, 19 (48%). Absence of neonatal seizures and/or a normal neurologic examination at discharge were significantly associated with good outcome.

Conclusion: For some term neonates the outcome of stroke may not be devastating. Predictions based on this data may assist in counselling of parents about individual prognosis.

L-10

Can Hypoxic-Ischemic Encephalopathy (HIE) Associated With Term Birth Asphyxia Lead to Mental Disability Without Cerebral Palsy?

C.M.T. Robertson (Edmonton, Alberta)

Background: Even with a non-disputed history of the occurrence of birth asphyxia, the childhood diagnosis of mental delay as an isolated disability, without cerebral palsy, is usually considered to be of antenatal onset. Surviving children with severe HIE often have multiple disabilities, including cognitive delay. Is this pattern of disability also true of survivors of moderate HIE of whom about 20% become disabled?

Methods: The Neonatal and Infant Follow-up Clinic, Glenrose Rehabilitation Hospital has assessed the development of survivors (>90%) of HIE in term newborns since 1974. Children with diagnosed syndromes or malformations of the central nervous system known to be associated with developmental delay are excluded. Outcomes of 407 prospectively identified survivors of moderate HIE is available. These survivors form 3 historical cohorts: born; 1974-79, 1982-86, 1987-96. The published data on the first two cohorts from school-age assessments has been combined (n=172). The third cohort, n=235, received assessments at 18-24 months. The population expected incidence of mental development of <50 is 0.13%, <70, 2.14%.

Results: Of the 172 school-age children, Wechsler Intelligence Testing identified 7 (4%) with scores <50 and 19 (11%) with scores <70 but without other disabilities. Of the 235 toddlers, the Bayley Scales of Infant Development identified 14 (6%) with indices <50 and 21 (9%) <70 but without other disabilities. Of the total of 40 mentally delayed children without cerebral palsy, hearing or vision loss, or epilepsy, 12 had the

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classical pattern of severe microcephaly beginning at birth and maximizing in the early months of life.

Conclusions: Isolated mental disability (<70) without other disabilities and not associated with known syndromes or malformations does occur in children with moderate HIE following birth asphyxia; it is 4.6 times more common than that expected for all causes of mental delay. Further investigation of the mechanism of this finding is required.

L-11

Anticardiolipin Antibodies are a Risk Factor for Recurrent Stroke in Children

S. Lindsay, G. deVeber (Toronto, Ontario)

Introduction: Anticardiolipin antibodies (aCL) have recently been recognized as being frequently present in children with arterial ischemic stroke (AIS) and sinovenous thrombosis (SVT). Such children may require anticoagulation treatment for secondary prevention. The clinical and radiographic features of ischemic stroke associated with aCL, particularly recurrence risk have not been delineated in large prospective studies.

Objective: To investigate, in a pediatric ischemic stroke cohort, the frequency of aCL and whether patients with aCL comprise a distinct clinical and radiographic syndrome, in particular a higher rate of multiple or recurrent..

Methods: We performed a single-center case (aCL +ve)-control (aCL -ve) study in 61 patients with AIS (n=47) and SVT (n=14) seen at the Hospital for Sick Children between January 1992 and January 1998.

Results: aCL occurred in 20/61 (33%) of our study group. Therefore, there were 20 cases (aCL +ve) (15 with AIS and 5 with SVT) and 41 controls (aCL -ve) (32 with AIS and 9 with SVT). Variables were analyzed with Instat 2.0 using Fisher's Exact test. In AIS, cases (aCL+) were significantly more likely to have multiple concurrent infarcts (n=9 cases; n=4 controls; p=0.001) and long-term recurrence of stroke (n=4 cases; n=1 control; p=0.030. In patients with SVT cases and controls did not differ for these variables. No significant differences were noted in: frequency of transient ischemic attack (TIA), migraine, family history of thrombosis, age, gender, preceding febrile illness, systemic thrombosis, or stroke type (AIS vs SVT).

Conclusion: ACL is frequent (33%) present in children with AIS and SVT and in AIS, is associated with increased risk of multiple initial infarcts and long-term recurrence. Further study regarding the role of anticoagulant treatment in these patients is indicated.

NEUROPHYSIOLOGY

M-02

^{1}H Nuclear Magnetic Resonance Studies of Pyridoxine-Induced Peripheral Neuropathy

R.L. Tyson, M. Hulliger, G.R. Sutherland (Calgary, Alberta)

Background: Excessive intake of pyridoxine (vitamin B_6) leads to a large-fibre peripheral neuropathy inducing severe motor deficits.

Methods: Cats (*N*=6) were given three doses (350mg/kg) of pyridoxine and allowed to recover for 3 weeks. Following this period, tissue samples from the central (frontal cortex, cerebellum, lumbar spinal cord) and peripheral nervous system (dorsal and ventral roots, medial gastrocnemius and superficial peroneal nerves) were obtained. ^{1}H nuclear magnetic resonance spectroscopy performed on perchloric acid extracts was used to measure *N*-acetylasparate (NAA) and *N*-acetylaspartylglutmate (NAAG) relative to *myo*-inositol.

Results: No changes in NAA or NAAG relative to controls were observed in CNS samples. Both NAA and NAAG were significantly decreased in dorsal roots and peripheral nerves, but not in ventral roots.

Conclusion: These data are consistent with a purely sensory fibre action of pyridoxine. We hypothesize that the pyridozine neurotoxicity is due to selective accumulation of pyridoxic acid, or another metabolite of pyridoxine, in peripheral sensory nerves. Such a build up would then inhibit multiple pyridoxal phosphate-dependent enzymes by competitive inhibition of the active coenzyme pyridoxal phosphate. The protection afforded by ventral roots may be due to the location of the cell body within the spinal cord.

M-03

Intraoperative Diaphragmatic Evoked Responses Following Transcranial Electrical Stimulation.

E. Weiss, D. Houlden, L. Burkholder, R. Midha, D.W. Rowed (Toronto, Ontario)

Surgery at the high cervical spinal cord and skull base may cause iatrogenic phrenic nerve injury or injury to the central respiratory pathways. Neuromonitoring of respiratory motor pathways during surgery is necessary to detect compromise to the phrenic nerve and allow for surgical measures that may reverse the compromise.

Multipulse transcranial electrical stimulation was performed on incomplete and complete cervical spinal cord injured patients undergoing surgery. Diaphragmatic motor evoked responses (MEPs) were recorded intraoperatively from surface electrodes placed over the costo-chondral junction of the 8 or 9th ribs bilaterally and the xiphoid process in three patients.

The stimulus threshold for the diaphragmatic response was 400 V and the responses obtained revealed a mean onset latency ranging from 18.0-23.2 ms with variable amplitudes dependent on stimulus parameters. Diaphragmatic responses were successfully obtained bilaterally from all patients. There was no intraoperative deterioration of the evoked diaphragmatic responses, and no new post-operative respiratory deficits.

The diaphragmatic MEPs obtained from complete spinal cord injured patients demonstrate the successful isolation of the hemidiaphragm response bilaterally. This suggests that diaphragm MEP monitoring is specific, and may be useful in monitoring central respiratory pathways and phrenic nerve function during surgery that puts them at risk.

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M-04

Use of Transcranial Electrical Stimulation to Assess Functional Status of Peripheral Nerve Motor Fibres During Brachial Plexus Surgery.

L. Burkholder, D. Houlden, E. Weiss, R. Midha (Toronto, Ontario)

Peripheral nerve grafting to a cervical nerve root is futile if motor fibres in the proximal stump have degenerated. Current intraoperative neurophysiological methods do not evaluate the integrity of motor fibres back to the anterior horn cell. Therefore, a technique that assesses functional status of motor fibres proximal to the brachial plexus exposure is necessary to avoid ineffective nerve grafting.

Studies were performed on a patient with an incomplete left brachial plexus injury. Directly stimulating and recording from selected exposed elements of the brachial plexus elicited nerve action potentials (NAPs). Somatosensory evoked potentials (SSEPs) were performed by directly stimulating the brachial plexus and recording from the scalp. Motor evoked potentials (MEPs) were performed by applying transcranial electrical stimulation and recording from the brachial plexus.

NAPs were present from the lateral and posterior cords after middle trunk stimulation but absent after upper trunk stimulation. SSEPs were present after medial cord stimulation but absent after stimulation of upper and middle trunks. MEPs were present from the medial cord but not the middle or upper trunk.

MEPs successfully evaluated functional status of motor fibres back to the anterior horn cell and coupled with NAPs and SSEPs allowed for accurate localization of the lesion sites.

M-05

EMG Findings in Postoperative Ulnar Neuropathy

Martin Veilleux (Montreal, Quebec)

Postoperative ulnar neuropathy is most likely localized at the cubital tunnel and results from poor positioning of the arm on the operating table. From 1995 until 1998, 13 patients were referred to the EMG Laboratory with a history of persistent numbness and weakness in the ulnar nerve distribution following surgery. There were 10 men and 3 women with a mean duration of symptoms of 8 months prior to EMG studies. The right hand was affected in 8, the left in 4 and both hands in 1. Findings on ulnar sensory nerve conduction studies (NCS) included no response in 7, reduced ulnar sensory nerve action potential (SNAP) amplitude in 6, and normal ulnar SNAP in 1. On ulnar motor NCS, there was no response in 1, reduced hypothenar muscle action potential amplitude in 7 and non localized slowing of the nerve conduction velocity in 8. Concentric needle examination showed denervation in the first dorsal interosseous muscle (FDI) in 8, chronic neurogenic motor unit potential (MUP) changes in the FDI in 10 and the flexor carpi ulnaris in 5. Although symptoms related to postoperative ulnar neuropathy were persistent, findings on EMG were of mild to moderate intensity.

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Poster Presentations

MOVEMENT DISORDERS

P-01

fMRI in Patients with Deep-Brain Stimulators (DBS): Application to Bilateral Deep-Brain and Cortical Surface Stimulators.

P.A. Pahapill, A.P. Crawley, K.D. Davis, A.R. Rezai, W.D. Hutchison, A.M. Lozano, D.J. Mikulis (Toronto, Ontario)

Background: Our recent work has investigated the safety and utility of fMRI in patients with unilateral thalamic electrodes for the treatment of chronic pain and tremor. The aim of this study was to: 1) further elucidate the utility of fMRI for assessing brain connectivity using electrodes as internal sources of neural stimulation, and 2) present results from the first cases of STN and cortical surface stimulation.

Methods: fMRI was performed using electrode stimulation in two patients; one with bilateral STN electrodes for advanced PD and one with a parietal cortical surface stimulating electrode for chronic pain secondary to a thalamic AVM that precluded standard thalamic DBS therapy.

Results: In the patient with bilateral STN electrodes, stimulation resulted in areas of activation immediately adjacent to the electrode terminus in the STN as well as the substantia nigra. In the patient with a single cortical surface electrode placed over M1/S1, activation of the anterior cingulum occurred in an area consistently activated with painful stimulation and/or focussed attention.[1]

Conclusions: This study further corroborates our previous work showing activation of known cortical connections from sites of direct deep brain stimulation indicating that DBS can be used to establish neural connectivity using fMRI.[2] Additional work promises to establish fMRI as a tool for studying the mechanism of action of these stimulators.

1. Davis KD, Taylor SJ, Crawley AP, Wood ML, Mikulis DJ. Functional MRI of Pain and Attention-Related Activations in the Human Cingulate Cortex. J. Neurophysiol. 77: 3370-3380, 1997.

2. Rezai A, Lozano A, Crawley AP, Joy MLG, Kwan CL, Davis KD, Dostrovsky J, Tasker R, Mikulis DJ. fMRI and Deep Brain Stimulation: Localization of Cortical and Sub-cortical Activation with Implanted Thalamic Stimulators (Accepted for publication March 1998, J. Neurosurg.)

P-02

Tremor Arrest with Thalamic Microinjections of Muscimol in Patients with Essential Tremor

P.A. Pahapill, R. Levy, J.O. Dostrovsky, K.D. Davis, A.R. Rezai, R.R. Tasker, A.M. Lozano (Toronto, Ontario)

Background: Thalamotomy and thalamic deep-brain stimulation (DBS) provide effective therapy for tremor. The therapeutic mechanism is unknown since neuronal cell bodies and fibers of passage can be affected in a non-selective manner. Our goal was to determine whether thalamic neuronal cell bodies are involved in the genesis of tremor by selectively inhibiting neurons at sites known to be good surgical targets for tremor therapy with stereotactic microinjections of the GABAA agonist muscimol.

Methods: In five patients undergoing unilateral stereotactic thalamic procedures for essential tremor (ET) muscimol was injected into the ventralis intermedius (Vim) thalamus in areas where tremor-synchronous cells were electrophysiologically identified with microelectrode recordings and where tremor reduction occurred with electrical microstimulation.

Results: Muscimol injections consistently reduced tremor in each patient.The effect had an average latency of 7 minutes and lasted an average of 9 minutes.

Conclusions: We propose that GABA-mediated thalamic neuronal inhibition may represent a mechanism underlying the effective surgical therapy for patients with tremor. To our knowledge, this is the first report of the physiologic effects of microinjection of a neurotransmitter analogue into the human thalamus. Muscimol injections could prove to be a useful tool in the investigation of the function of specific brain sites in humans during functional stereotactic surgery and may represent a novel strategy to treat ET and other disorders characterised by neuronal dysfunction.

P-03

BOTOX® (Botulinum Toxin Type A) Purified Neurotoxin Complex Prepared from the New Bulk Toxin Retains the Same Preclinical Efficacy as the Original but with Reduced Immunogenicity.

K.R Aoki, G. Merlino, A. Spanoyannis, L. Wheeler (Irvine, California)

Background: In 1997, the USFDA approved a new bulk toxin source for use in the production of BOTOX®. Although comparable to the original in all other ways, this “new” BOTOX® has a 6-fold lower neurotoxin protein load, but the same number of units (100) per vial. This study compares the muscle weakening efficacy and the immunogenicity of new BOTOX® to original BOTOX®.

Methods: The Digit Abduction Scoring Assay in mice was used to compare muscle weakness. To compare immunogenicity, rabbits were treated monthly with 3 units/kg, i.m. for 8 months. Serum was evaluated for anti-type A neurotoxin antibodies in vitro, and for neutralizing antibodies using the mouse protection assay.

Results: Both BOTOX® products produced identical dose-related muscle weakness in mice. Original BOTOX® elicited neutralizing antibodies in rabbits by month 3. New BOTOX® did not elicit any detectable in vitro or neutralizing antibodies up to month 8.

Conclusions: These results demonstrate that, in rabbits, the lower neurotoxin protein load of new BOTOX® resulted in significantly less neutralizing antibody formation than original BOTOX® without affecting the muscle weakening effect in

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mice. This may reduce the risk of antibody formation during clinical use of BOTOX® and may have implications for evolving treatment paradigms.

P-04

Reversible Parkinsonism of Rapid Onset Induced by Valproate

C. Chayer, M. Freedman (Toronto, Ontario)

Background: Valproate is becoming a more frequently used drug. Indications include epilepsy, bipolar affective disease, chronic pain, migraine and control of agitation and aggression in patients with brain-damage. Parkinsonism has been reported as a rare side effect following chronic use in patients with epilepsy.

Method: We report two patients who developed parkinsonism while being treated with valproate for mania.

Results: Case 1 is an 80 y.o. woman with a severe head injury and resultant cognitive deficits due to right fronto-temporal and left parietal lesions. She developed secondary mania for which valproate was started. She developed rigidity and reduced ambulation after two months of treatment. This resolved three months after the valproate was stopped. Case 2 is a 74 y.o. woman with vascular dementia and secondary bipolar affective disorder who showed signs of parkinsonism (shuffling gait, bradykinesia) after three months on valproate. Significant improvement in her walking was seen one month after discontinuation of the drug.

Conclusion: Parkinsonism may develop after short-term exposure to valproate. Predisposing factors for the relatively rapid development of parkinsonism on valproate may include pre-existing central nervous system pathology and aging. These factors should be considered when choosing valproate for neurological and psychiatric disorders.

P-05

A Randomized Double-Blind, Placebo-Controlled Crossover Trial of Botulinum Toxin in Chronic Whiplash Pain - A Pilot Study

Anne-Louise Lafontaine, Oksana Suchowersky, Shyamal Das and Rollin F. Brant. (Calgary, Alberta)

Objective: To examine the efficacy of Botulinum toxin (Botox) in chronic whiplash pain as compared to normal saline (placebo).

Background: Whiplash injury is a symptom complex, resulting from soft tissue trauma to the neck following rear-end collision. The pathology of whiplash injuries remains uncertain however, injuries to the neck muscles, including stretching, tearing and hemorrhaging have all been postulated. Botox has been used therapeutically in the last decade for the relief of pain and abnormal movement associated with cervical dystonia. More recently, a randomized study has shown the efficacy of Botox in the treatment of myofascial pain syndrome. To date, no studies have evaluated its efficacy in whiplash injury.

Design/Methods: A double-blind, placebo controlled, crossover trial was used to evaluate the efficacy and tolerability of Botox in the treatment of chronic whiplash pain. Subjects received 2 injections in random order of either Botox or normal saline. A total of 150 mouse units or the equivalent volume of saline was injected in 4 standardized sites along the upper trapezius muscle. Subjects were evaluated at weekly intervals for 4 weeks, then at 8 weeks and at 12 weeks after each injection. The primary assessment outcome was the Visual Analogue Scale (VAS) of pain and general well being. Secondary outcome assessments were the Visual Analogue Scale of level of activity, the patient global assessment as per the Quebec Task Force Protocol, and the patient global assessment of efficacy.

Results: A total of 12 subjects met the inclusion criteria. Preliminary results are available for 9 patients with one month of follow-up. The VAS of pain score improved in 77.8% (7/9) of the patients in the placebo group compared to 66.7% (6/9) in the Botox group. The VAS of well being score improved in 37.5% (3/8) of the patients in the placebo group compared to 33.3% (3/9) in the Botox group. The VAS of activity level score improved in 66.7% (6/9) of the patients in the placebo group compared to 33.3% (3/9) in the Botox group.

Conclusions: Preliminary examination of the data reveals no evidence to suggest that Botox influenced patients experience of pain and well being. Unexpectedly, activity level decreased after Botox injections.

NEUROPHYSIOLOGY

P-06

Malignant Rolandic-Sylvian Epilepsy (MRSE); Magnetoencephalography, Invasive Intracranial Video EEG Monitoring and Surgical Treatment

H. Otsubo, A. Ochi, I. Elliot, V. Jay, J.T. Rutka, M. Smith, OC. Snead III (Toronto, Ontario)

Background: Within rolandic epilepsy, patients with intractable seizures, neuropsychological deficits and a variety of central-temporal spikes have been reported. We present non-lesional 6 patients with malignant rolandic-sylvian epilepsy (MRSE) who underwent invasive intracranial video EEG (IVEEG) monitoring and surgery.

Methods: Six children (age 5-15 years) were evaluated using prolonged video EEG telemetry (scalp and subdural electrodes), MRI, MEG and neuropsychological assessments.

Results: Seizure onset varied between 1 and 5 years, consisting of generalized seizures with sensory aura, facial twitching and arm posturing in 2 each. MEG showed spikes on peri-sylvian (2) and peri-rolandic fissure (4). IVEEG revealed ictal onset zone around peri-sylvian (2) and peri-rolandic fissure (4). After cortical excision and multiple subpial transection, 3 were seizure free, 3 showed improvement. Preoperatively, 4 with left hemisphere abnormality showed neuropsychological deficits. Two of them showed an increase in attention problems postoperatively. Two with right hemisphere abnormality showed

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normal (1) and deficits (1) in neuropsychological performance without change after surgery.

Conclusion: MRSE presents intractable seizures, neuropsychological problems and the epileptogenic zone in rolandic-sylvian fissures, and is surgically treatable. MEG is a valuable diagnostic method to localize spike field for MRSE and may delineate functional and epileptic zone prior to surgery.

P-07

Monomelic Amyotrophy Presenting As Isolated Thenar Wasting After a Fall

T. Miller, J. Roth, (London, Ontario) A. McComas, (Hamilton, Ontario)

Juvenile muscular atrophy or benign focal amyotrophy have principally been reported in Japan and India. We report an unusual case with discussion of rehabilitation. An 18-year-old caucasian male fell on his outstretched right hand while roller blading. No fracture was identified but the patient persisted with hand and thumb pain associated with use and thenar atrophy. Clinical findings revealed pain and tenderness at the base of the thumb with marked thenar eminence atrophy. No other atrophy or weakness was identified. Sensory examination was normal. MRI (cervical spine) was largely within normal limits except for slight atrophy of the cervical cord. Serial neurophysiology over a 2 year period revealed severe loss of functioning motor limits in the right thenar eminence and subtle chronic changes in the left C8 myotome. Sensory potentials were of normal amplitude and latency. CT scan of the hand revealed degenerative (subchondral cysts) changes in the scaphotrapezium joint. The electromyographic findings of neurogenic atrophy with slow progression and then arrest, are most consistent with the rare condition of monomelic amyotrophy. A discussion of monomelic atrophy and the management of his thumb atrophy is presented.

P-08

Proximal Median Neuropathy Secondary to Humeral Fracture

Martin Veilleux, and Peter Richardson. (Montreal, Quebec)

Median neuropathies proximal to the wrist are uncommon and result from penetrating injuries, compression by muscles, fibrous bands or ligaments, fracture dislocation of the distal humerus, or a fall on the shoulder or arm. A 66-year-old man fell down the stairs on July 15, 1998 and suffered a comminuted fracture of the right proximal humerus that required internal fixation on July 19. Even prior to surgery, he noted hyperesthesia on the tip of the thumb and index finger and weakness of the thumb and index flexor muscles. Neurological examination at the time of the EMG on September 1 revealed weakness of the abductor pollicis brevis (APB), flexor pollicis longus (FPL) and flexor digitorum profundus (median head) 1/5 and a marked hyperesthesia of the tip of the thumb and index finger. Nerve conduction studies showed no response on median motor nerve stimulation and a markedly reduced median sensory nerve action potential (SNAP) amplitude. Concentric needle examination of the APB and FPL muscles revealed numerous fibrillations and a marked loss of motor unit potentials (MUPs) while in the pronator teres, there was extensive denervation and no activation of MUPs. Surgical exploration showed median nerve compression by fibrous band in the upper arm. Proximal median neuropathy can occur in proximal humeral fracture.

EPILEPSY

P-09

Automatisms in Cardiogenic Syncope Mimicking Partial Complex Epilepsy.

Michael D.Hill, Arline McLean (Toronto, Ontario)

Background: Automatisms are common in temporal lobe epilepsy. We present an instructive case of syncope induced automatisms mimicking partial complex epilepsy.

Methods: Case report.

Results: A 78-year-old man with multi-infarct dementia, began having unusual spells. He became verbally unresponsive with tonic posturing of his arms and chewing movements lasting 5-30 seconds without apparent post-ictal state, occurring up to 25 times per day. Between spells his neurological status rapidly returned to baseline. Examination revealed pseudobulbar palsy and bilateral Babinski signs. An ECG showed sinus arrhythmia. Two EEG recordings showed non-focal slowing. Valproate was started and titrated to therapeutic drug levels, but had no effect. During a third EEG a 10 second spell occurred (videotape segment). The ECG tracing demonstrated asystole. Sick sinus syndrome was diagnosed and he is now completely asymptomatic after pacemaker insertion.

Conclusions: Syncope may result in a short generalized convulsion mimicking a tonic-clonic seizure. Seizures may induce syncope, tachyarrythmias and even sudden death. We speculate that a previous small infarct, perhaps involving the supplementary motor area, was an epileptic focus and discharged under conditions of hypoxia resulting in the observed "seizures". It remains possible that these movements are not epileptic per se.

P-010

Ictal Experiential Hallucinations

A. Ogunyemi (St. John's, Newfoundland)

Background: Since the classic observations of Ponfield regarding experiential hallucinations; the phenomenon has continued to intrigue neuroscientists. The majority of the patients studied however, have had complicated seizure manifestations.

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This report describes four patients having simple partial seizures manifesting with experiential hallucinations.

Methods: Among the patients attending the Seizure Clinic, St. John's, Newfoundland, we identified four having simple partial seizures with experiential hallucinations. They did not have associated visceral or affective symptoms. Neurological examination, MRI scan of the brain and EEGs were accomplished for all of them. They have been followed in the clinic for 3 to 12 years.

Results: The patients consist of one man and three women with ages ranging between 25 and 37 years. The man has post-traumatic epilepsy having sustained left fronto temporal contusion at the age of 9 years. One woman had a large left trigeminal schwannoma. The other two women had normal MRI scans of the brain. The EEGs showed left frontal spikes in one patient and left anterior temporal spikes in the other three.

During seizures, two patients have vivid visions of scenes from television cartoon programs: "GI Joe", and "The Big Comfy Couch"; another patient visualizes scenes from "Star Wars". The fourth patient finds herself at a specific location in a distant country where she had resided for 2 years.

All of them experienced speech arrest and two had drooping of the right side of the face during the seizures.

Conclusion: Detailed clinical assessment accords with the notion that both the mesial temporal structures and the fronto temporal neocortex are activated during seizures with experiential hallucination. The epileptiform activities may be lateralized to the left (dominant) cerebral hemisphere.

P-011

Adult On-set Secondary Generalized Epilepsy (Lennox-Gastaut Syndrome) in Patients with Down's Syndrome.

A Ogunyemi (St. John's, Newfoundland)

Background: Lennox-Gastaut syndrome is regarded as an age-related epilepsy syndrome. The onset of seizures occurs between age 1 and 8 years. There is paucity of information about the characteristic triad of Lennox-Gastaut syndrome emerging among adult patients with Down's syndrome.

Methods: Two patients with Down's syndrome, a man and a woman who are 26 and 47 years old respectively, began to have seizures 5 years ago. Both of them are followed at the Seizure clinic, St. John's. Neurological examination, CT scan and MRI scans of the brain as well as serial EEGs were accomplished for both of them.

Results: They both have multiple seizure types consisting of atypical absence, generalized tonic clonic, tonic and atonic seizures. Their EEGs showed slow background rhythms, generalized spike and wave and generalized slow spike and wave. CT and MRI scans were unremarkable.

Accelerated cognitive decline was coincident with the onset of epilepsy in both of them. Treatment with antiepileptic medications resulted in seizure control and improvement in cognitive ability.

Conclusions: The triad constituting Lennox-Gastaut syndrome may result when severe disease of sufficient duration involve the cerebral cortex diffusely, irrespective of the age of the patients. Adequate antiseizure treatment may stem the cognitive decline and control the seizures.

P-012

Intractable Late Onset Frontal Lobe Epilepsy after "Minor" Head Trauma in Childhood

R. Sadler (Halifax, Nova Scotia), R. McLachlan (London, Ontario)

Background: The risk of developing post-traumatic epilepsy is directly proportional to the severity of injury with most developing seizures within 5 years of injury. We identified 3 adult patients who developed medically resistant epilepsy several years following what was initially believed to be an irrelevant head injury.

Results: Male=2 (32,38 years), female=1 (24 years). Age at time of trauma = 6-8 years. Patient 1 was hit by a car; patients 2 and 3 were struck by baseball bats. None of these patients lost consciousness, had any immediate sequelae of a concussion or peritraumatic amnesia. Patient 1 had a linear skull fracture and was observed in hospital overnight; patient 2 had a minor depressed skull fracture but no dural laceration; patient 3 did not seek medical attention. The first recognized seizure occurred after latencies of 6, 10, and 12 years respectively. The predominant seizure types were secondarily generalized tonic-clonic seizures (patients 1, 3) and partial complex seizures (patient 2). All patients had normal neurologic examinations. Seizures were resistant to 4-6 antiepileptic drugs. All patients had large areas of right frontal encephalomalacia on MRI scans. All are seizure free, or nearly seizure free, after right frontal resections (follow-up = 3-15 months).

Conclusions: Highly epileptogenic lesions may develop in the frontal lobe after what may be initially interpreted as "minor" head trauma in young children. These lesions respond favourably to surgical interventions

P-013

A Case of Cardiac Sequelae of Prolonged Seizure Activity

K. Butcher, M. Javidan (Edmonton, Alberta)

A 64-year-old woman developed a seizure disorder secondary to a right sided subarachnoid hemorrhage 7 years prior to admission. She experienced generalized tonic clonic seizures and one witnessed left sided focal seizure. A previous EEG demonstrated marked slowing over the right hemisphere. On the day of admission, the patient was witnessed to be in status epilepticus for approximately 1 hour.

On examination deep tendon reflexes were increased on the left. Plantar responses were extensor on the left and flexor on the right. 48h after admission, the patient complained of dull left sided chest pain. An ECG showed T wave inversion in the inferolateral leads. Cardiac enzymes were elevated and a presumptive diagnosis of myocardial infarction was made. An angiogram

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showed only non-significant stenotic lesions. A large akinetic area was visible, confirming cardiac damage. An EEG showed significant pleomorphic lateralizing epileptic discharges, mainly in the right hemisphere.

This most likely represents cardiac damage secondary to sympathetic overdrive following prolonged seizure activity. The history, physical findings and EEG suggest the seizure's focus is in the right hemisphere. Similarly, stimulation of the right insular cortex, in epilepsy patients undergoing ablative surgery, results in mainly sympathetic responses, while parasympathetic effects are seen with left insular stimulation. This case emphasizes the need to be aware of possible cardiac consequences of epilepsy and provides further evidence for right hemispheric predominance of sympathetic cardiac effects.

P-014

The First Canadian Questionnaire Survey of Knowledge and Attitudes Regarding Epilepsy and Persons with Epilepsy

B. Young, S. Wiebe, P. Derry, I. Hutchinson, L. Brown and M-L Matthews, (London, Ontario)

Background: No previous Canadian study assessed knowledge and attitudes of young adults regarding epilepsy

Methods: A voluntary, standardized questionnaire was given to students in an introductory college psychology class.

Results: Of 65 students (100% compliance; females:males = 39:16; mean age = 21.9 [SD 5.5] years), 5 % had ≥1 seizure after age 5 years; 60% knew persons with epilepsy; 47% witnessed ≥1 seizure; 85% read about epilepsy. The following were recognized as causes of epilepsy: trauma by 6%, brain tumors 35%, stroke 33%, birth trauma or defects 33%, insanity 13%. Knowledge of seizure phenomena: convulsive movements 91%, nonconvulsive loss of consciousness 53%, behavioral change 29%, memory disturbance 33%. Ninety-one % thought antiepileptic drugs (AED) were effective; 98% knew AEDs should not be stopped abruptly. Seven % recognized potential AED teratogenicity. Seven % objected to their (eventual) children associating with someone with epilepsy; 2% objected to close family members marrying persons with epilepsy; 9% thought persons with epilepsy should not have children; 85% thought capable persons with epilepsy should be employed.

Conclusions: Students showed excellent compliance for questionnaire completion; about half had first hand knowledge about epilepsy; despite patchy knowledge, tolerant attitudes prevailed. Results compare favorably with studies from other countries.

P-015

An Evaluation of TOPAMAX® tablets in Subjects with Treatment-Resistant Epilepsy.

J. Schneiderman (Toronto, Ontario), G. Baker (Liverpool, England)

Background: This open, multicentre study was designed to evaluate the efficacy and safety of TOPAMAX* tablets in subjects who were not satisfactorily controlled with conventional therapy. The impact TOPAMAX* had on quality of life was also examined.

Methods: Two-hundred and five subjects with various types of epilepsy and who had at least six seizures during a 12-week retrospective baseline were enrolled in the study.

Results: Seventy-four percent of the subjects completed the 6-month trial. Forty-four percent of the subjects reported a 50 % or greater reduction in seizures from baseline, while 10 % of subjects were seizure free during this same period. Over 53 % of subjects were rated by the Investigators as having achieved moderate or marked improvement. Sixty-three percent of the subjects continued on TOPAMAX* after the study ended. Quality of life data will be presented. The most commonly reported adverse events were; headache, fatigue, weight decrease, dizziness and difficulty with concentration. Only 14 % of the subjects discontinued TOPAMAX* due to adverse events. The weight loss averaged 3.5 kg over the course of the study.

Conclusions: TOPAMAX* was efficacious and well-tolerated in subjects with treatment-resistant epilepsy.

P-016

Dipole Source Localization of Epilepsia Partialis Continua in a Patient with Rasmussen's Syndrome

A. Ochi, H. Otsubo, A. Hunjan, R. Sharma, M. Bettings, OC. Snead III (Toronto, Ontario)

Background: Dipole source localization (DSL) method has been used to localize a generator site of cortical myoclonus in epilepsia partialis continua (EPC). We analyzed the DSL of individual EEG spikes preceding the myoclonus during EPC and compared them to interictal spikes (iiS) in a patient with Rasmussen's syndrome (RS).

Methods: A 7 year-old girl had presented with EPC consisting of left arm and leg twitching and progressive hemiparesis since the age of 5. Video EEG telemetry was performed with 19 scalp electrodes and EMG (left thenar and anterior tibial muscle). We analyzed DSLs using a single moving dipole on a three-shell spherical model, overlaid onto co-registered MRI (SynaPoint, NEC, Japan).

Results: We obtained 7, 2, and 7 DSLs which showed goodness of fit>98% among 20 hand, 19 leg myoclonic spikes, and 40 iiS, respectively. The 9 DSLs with myoclonus were localized in the right precentral region, deeper subcortical regions compared to scattered and superficial DSLs of iiS around central cortex. The DSLs of the hand jerks corresponded to hand motor area on fMRI.

Conclusion: The DSLs with cortical myoclonus in RS were localized deeper and concentrated in the precentral region, and considered to be an ictal symptomatogenic zone.

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P-017

Surgical Outcome in Patients with Tuberous Sclerosis

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Introduction: Tuberous Sclerosis (TS) has proven to be a clinically heterogeneous disorder. A minority of patient have the classic triad of adenoma sebaceum, mental retardation and seizures, while 80% of patients have epilepsy. Epilepsy surgery is rarely considered for these patients as most have multiple intracranial tubers. However, a subset of TS patients with medically refractory epilepsy may benefit from surgical resection of their epileptogenic focus. *Methods:* We have retrospectively reviewed 7 patients with TS and medically refractory seizures admitted to the Comprehensive Epilepsy Program at the University of Alberta who underwent surgical resection of an epileptogenic focus. All patients underwent extensive preoperative assessments including seizure charting, EEG, long term video EEG monitoring, CT, MRI and neurodevelopmental assessments. *Results:* Patients ranged in age from 15 months - 14 years (mean 6 years). Follow up ranged in duration from 6 months to 10 years (mean 4 years). Five patients had complex partial seizures and 2 patients had infantile spasms. One of the patients with infantile spasms also had simple partial seizures and secondarily generalized seizures. Three patients had temporal lobectomies and three had lesionectomies (removal of a single hamartoma/tuber) and one had both a temporal lobectomy and a lesionectomy. All 7 patients are seizure free. The patients with infantile spasms had normalization of their EEG and cessation of their spasms. *Conclusion:* TS is a heterogeneous disorder with seizures as a predominant symptom. Properly selected patients with appropriate electroencephalographic, clinical and radiographic features may benefit from a resection of their epileptogenic focus.

P-018

Recording of Single Ion-Channel Activity in Human Neocortical Slices from Epileptic Patients

P.A. Pahapill, M. Pelletier, A.M. Lozano, S.S. Jahromi, L. Zhang, P.L. Carlen (Toronto, Ontario)

Background: Understanding altered neuronal ion-channel activity responsible for epileptogenesis is essential for elucidating the neuronal mechanisms underlying epilepsy and for directing rationales designed to develop new pharmacotherapeutic agents. Thus, direct studies of the neurophysiological properties of ion channels in human brain cells is essential. There have been no reports of single ion-channel activity from human brain tissue. Our goal was to record single ion-channel activity in human brain cells under physiological conditions.

Methods: Single ion-channel activity was studied in human brain cortical slices prepared from patients undergoing surgical treatment for medically intractable temporal lobe epilepsy. Usinig standard "patch-clamp" techniques, high-resistance "giga-ohm" seals were obtained in the "cell-attached" recording mode.

Results: Single ion-channel activity recordings were obtained in acutely isolated human brain cortical slices. Preliminary results have shown voltage-independent single ion-channel activity with conductances of 50 pS and 200 pS.

Conclusions: With "patch-clamp" techniques we have been able to record single ion-channel activity in human brain cortical slices. Recordings in the "cell-attached" mode are more physiological than "whole-cell" or isolated membrane patch recordings since cell integrity is maintained. To our knowledge, this is the first report of recordings of single ion-channel activity from the human brain. Direct electrophysiological studies of single ion-channel activity in human brain tissue are important for understanding the fundamental mechanisms underlying epilepsy and other neurological diseases and their responses to neuroactive drugs.

P-019

Partial Status Epilepticus in Benign Rolandic Epilepsy: The Anterior Operculum Syndrome

D. Gregory, K. Farrell, P. Wong, M. Connolly (Vancouver, BC)

Background: Partial status epilepticus occurring in patients with benign rolandic epilepsy may manifest as the anterior operculum syndrome.

Methods & Results: This 4-year-old boy had a history of simple partial seizures involving facial twitching and postictal dysarthria. Interictal EEGs showed independent bilateral centrotemporal spike discharges with a frontotemporal dipole field. Over a two-week period, the child developed persistent drooling, dysarthria and poor head control. An EEG demonstrated an increased frequency of the centrotemporal discharges. When the discharges occurred at higher frequencies (2/sec), episodes of speech arrest and head nodding occurred. The ictal discharges had the same centrotemporal configuration, were of high voltage (700-900 uV), and could be blocked by asking the child to stick out his tongue or by touching the contralateral lip. Intravenous Diazepam blocked the discharges and was associated with improvement in speech and drooling.

Conclusion: This child demonstrates the clinical features of the anterior operculum syndrome. In contrast to the reported ictal correlate of benign rolandic seizures, the EEG correlate comprised repetitive focal spikes with the same field and polarity as interictal spikes in benign rolandic epilepsy. The high voltage, diffuse field and continuous nature of the discharges may be misinterpreted as continuous spike-wave during slow sleep.

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P-020

An Open Design Study to Evaluate the Impact of Add-on Lamictal (lamotrigine) on the Quality of Life of Patients with Epilepsy

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Background: Epilepsy is a disorder which has been shown to effect patients' health-related quality of life (HRQL). This study assesses the impact of add-on Lamictal on the HRQL of epilepsy patients.

Methods: A prospective, open-label study was conducted across Canada. Patients with uncontrolled epilepsy receiving treatment with at least one anti-epileptic medication were enrolled. A stable dose of 50-250mg BID of Lamictal was administered as add-on. HRQL was measured using the Quality of Life in Epilepsy (QOLIE)-31 questionnaire. The patients' seizure frequency and adverse experiences were also collected.

Results: 188 patients entered the study, of which 185 patients 18-65 (mean 38) years of age provided data for analysis. After initiation of Lamictal as add-on therapy, seizure frequency was reduced from a mean of 26 seizures per 8-week period at baseline to 16 seizures after 24 weeks of treatment. 38 patients became seizure free. Adverse events reported were similar to previous studies. Overall QOLIE-31 scores improved by 6 points after 24 weeks of Lamictal therapy. Statistically significant improvements were seen in all subscales of the QOLIE-31.

Conclusions: Add-on Lamictal therapy was effective in reducing seizure frequency and improving HRQL of adults with uncontrolled generalized and partial seizures.

P-021

Antiepileptic Drug Withdrawal, Blood Levels and Occurrence of Seizures in a Video-EEG Monitoring Unit.

M. Charest, R. Desbiens, J. Roy, L. Nadeau (Quebec City, Quebec) S. Tremblay (Chicoutimi, Quebec)

Background: Antiepileptic drug (AED) withdrawal during EEG-video monitoring is important for the evaluation of epilepsy surgery candidates. Whether the first seizure occurs during the fall of AED blood levels or during low stable levels is controversial. Our study is an attempt to clarify this question.

Methods: Blood levels of AEDs were measured daily and were correlated with the timing of the first seizure in 27 epileptics undergoing intensive video-EEG monitoring. Drug tapering was rapid and included, in most cases, more than one AED.

Results: Twenty-one out of 27 patients (78%) had their first seizure during the fall of drug levels; in 3 it occurred during the low-stable phase, and 3 had different patterns of seizure occurrence. These differences were statistically significant (x^2= 8,33). In most cases, the first seizure happened when blood levels were still in the therapeutic range. By day 4, 86% had their first seizure.

Conclusions: In the setting of AED withdrawal for video-EEG monitoring, the first seizure has a tendency to occur during the rapid fall in blood levels. This finding will help the clinician in choosing the appropriate rate of AED withdrawal in such a situation.

DEMENTIA

P-023

Neurostimulation of the Medial Septal Nucleus in Alzheimer's Disease.

J. Turnbull, W. Molloy, K. Reddy, F. Jiang. (Hamilton, Ontario)

Background: The septal nuclei facilitate normal learning and memory through uncertain mechanism(s). They may serve as an essential relay between the midbrain and the hippocampi in arousal, and they may play an essential gating, clocking, or synchronizing function. The cholinergic septal projections to the hippocampi are severely affected in Alzheimer's disease, and there is decrease in hippocampal acetylcholine levels. Septal stimulation in adult rabbits increases hippocampal choline acetyltransferase activity and acetylcholine levels, and stimulation of the septal nuclei in aged rats significantly improves performance in a spatial maze. With the support of our institutional ethics review board, we implanted a neural stimulator in the medial septal nucleus of a patient with terminal AD, consistent with the family's wish, and the patient's previously-voiced wish, to try experimental treatment. The patient had not spoken for several months, was bed ridden, and could not toilet or feed herself. Aricept was unhelpful.

Methods: A Medtronix neural stimulating electrode was inserted into the medial septum using stereotactic techniques, after MRI localization. Stimulation was undertaken at a number of frequencies and intensities.

Results: Stimulation produced transient but somewhat remarkable results. The patient was more alert, and became more fluent of speech. However, the benefit was short lived. At no point was there evidence of seizures or kindling. The patient subsequently succumbed of her disease. A post mortem examination confirmed severe AD, showed excellent electrode position, and no evidence of stimulation damage.

Conclusion: Medial septal stimulation is well tolerated but of transient benefit in severe AD.

The support of the DeGroote Foundation is gratefully acknowledged. Medtronix provided technical support and the stimulator.

P-024

Using A Combined Randomized Start/Withdrawal Design to Assess Propentofylline's Effect on Disease Progression in Alzheimer's Disease and Vascular Dementia

B. Kittner (Bridgewater, New Jersey) for the European/Canadian Propentofylline Study Group

Background: Previous phase II and III trials have shown that

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propentofylline improves cognitive performance and global function in patients with Alzheimer's disease (AD) and/or vascular dementia (VaD). The ability of propentofylline to slow the progression of dementia was suggested by a phase III trial in which treatment effects were maintained for up to 8 weeks after cessation of active drug therapy. Two studies (MN 304 and MN 305) using a combined delayed-onset/withdrawal design were conducted to further explore propentofylline's effect on the underlying course of dementia.

Methods: Patients with mild-to-moderate AD were enrolled in study 304 and patients with probable or possible VaD were enrolled in study 305. In segment I (48 weeks in study 304, 24 weeks in study 305), patients were randomized to propentofylline or placebo. During segment II (24 weeks in both studies), half of the propentofylline patients from segment I were switched to placebo (withdrawal segment) and half continued receiving propentofylline. Similarly, half of the placebo patients from segment I were switched to propentofylline (delayed-onset segment) and half remained on placebo. If the treatment differences achieved at the conclusion of segment I are maintained during segment II (continuous placebo vs. propentofylline-to-placebo for withdrawal analysis; continuous propentofylline vs. placebo-to-propentofylline for delayed-onset analysis), an effect on disease progression can be inferred.

Results and Conclusions: Results and conclusions will be reported at the meeting.

Supported by: Hoechst Marion Roussel, Inc.

BASIC NEUOSCIENCES

P-025

Does Ischemia Contribute to Poor Regeneration After Chronic Denervation in Peripheral Nerves?

A. H ke, H.S. Sun, T. Gordon and D.W. Zochodne (Calgary, Alberta)

Background: Regeneration in the peripheral nervous system (PNS) after injury is usually very robust. However, if a distal denervated segment remains denervated for a prolonged time, regeneration into this segment is poor. In order to test the hypothesis that chronic ischemia may contribute to this poor regeneration, we evaluated local perfusion in a chronically denervated nerve over time.

Methods: After a unilateral sciatic nerve transection in adult rats, regeneration of the proximal nerve was prevented by suturing it into nearby muscles. Over 6 months, at different time points blood flow measurements were done in both the denervated nerve and the contralateral sham operated nerve using both laser doppler flowmetry (LDF) and microelectrode hydrogen clearance polarography (HC).

Results: Following transection there was early hyperemia (2-14 days) followed by a dramatic decrease in endoneurial blood flow (as measured by HC) by 3 and 6 months in the distal stump. This decrease in endoneurial blood flow was accompanied by a decrease in RBC flux measured by LDF indicating declines in epineurial/perineurial perfusion.

Conclusions: The findings identify a decline in the perfusion of chronically denervated nerve trunks. The changes might render an unfavorable environment for late reinnervation, or reflect a response to a reduction in local metabolic demand.

P-026

Peripheral Nerve Regeneration in Experimental Diabetes Mellitus

J. Kennedy,D.W. Zochodne (Calgary, Alberta)

Background: Diabetes mellitus may adversely influence the regeneration of an injured peripheral nerve. The mechanisms are unknown. This study was conducted to evaluate nerve regeneration in an experimentally-induced mouse model of diabetes mellitus.

Methods: Diabetes was induced in Wistar mice by streptozotocin (in citrate buffer) injection while controls received the buffer alone. Left sciatic nerves were crushed after 4 weeks. Over 0-8 weeks we measured sciatic motor fiber reinnervation of foot interosseous muscles (M, or compound muscle action potential), conduction of intact motor and sensory fibers and autotomy behaviour.

Results: As expected, noninjured diabetic sciatic nerves developed slowing of conduction velocity but M-potentials were unchanged. Diabetics had delays in the recovery of the M-potential and of conduction velocity in sciatic fibers that were prominent 3-6 weeks following crush, then resolved. Diabetic animals also demonstrated a dramatic rise in autotomy behaviour, suggesting increased neuropathic pain.

Conclusions: Diabetic motor fibers have delayed reinnervation that is prominent 3-6 weeks following a nerve crush. This delay is also associated with enhanced neuropathic pain.

P-027

Enzyme Kinetics of Butyrylcholinesterase and Trypsin: Implications in Alzheimer's Disease

S. Darvesh, R. Kumar, E. Martin (Halifax, Nova Scotia)

Background: Butyrylcholinesterase (BuChE) is an enzyme involved in cholinergic neurotransmission which is also found in neuritic plaques in the brains of patients with Alzheimer's disease (AD). Because brain-specific trypsin has been implicated in amyloid precursor protein processing and trypsin-like activity co-purifies with BuChE, enzyme kinetic studies were used to examine BuChE-trypsin interactions.

Methods: Kinetic properties of trypsin-like activity associated with BuChE or trypsin were determined by using Nα-benzoyl-DL-arginine-p-nitroanilide (BAPNA), a site-specific substrate for trypsin. BAPNA was incubated with trypsin or BuChE or a

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mixture of the two enzymes, with and without the BuChE inhibitor ethopropazine. The product p-nitroaniline (PNA) was measured by using high performance liquid chromatography and its rate of formation, as well as substrate affinity (Km) and activation (K_{act}) constants were determined.

Results: Incubation of BAPNA with a mixture of trypsin and BuChE led to a 3- to 5-fold increase in the rate of product formation as compared to either enzyme alone. Increasing BuChE caused progressive stimulation of BAPNA hydrolysis. Addition of ethopropazine to BuChE led to a concentration dependent stimulation of BAPNA hydrolysis, an effect not observed with trypsin alone.

Conclusions: BuChE has a stimulatory effect on the activity of trypsin. Therefore, BuChE may participate in AD pathophysiology through loss or enhancement of the synergistic effect of BuChE on enzymes such as trypsin. Inhibitors of BuChE may have an effect on modifying AD pathology.

P-028

Extended Opportunity of 'Therapeutic Window' by 6-h Delayed Intravenous Perfusion of Magnesium Sulfate after Focal Middle Cerebral Embolization in Rat.

Y. Yang, Q. Li, F. Ahmad, A. Shuaib, (Edmonton, Alberta)

Magnesium has been shown to be neuroprotective in both global and permanent focal ischemia animal models. However, to date, the efficacy and the 'therapeutic window' of magnesium have never been examined in an animal model of focal ischemia systematically. The present experiments were designed to investigate these. Focal middle cerebral artery occlusion was accomplished by introduction of an autologous thrombus into the right middle cerebral artery via the internal carotid artery. Wistar rats were randomly grouped (n=10 in each group) and dosed with vehicle or 5% magnesium sulfate at 90 mg/kg (i.v.) at 2h, 6h, and 8h after introduction of embolus. Postmortem infarct volumes were determined by quantitative image analysis from 2,3,5-triphenyltetrazolieum chloride (TTC) stained coronal slices at 72 h after the embolization. Neurological outcome and survival rates were also observed and compared before and after treatment or between groups. Magnesium treatment at 2h or 4h after cerebral embolization resulted in an increase in survival rate of animals. Animals treated with vehicle or magnesium at 8h after ischemia did not improve neurological scores. In contrast, neurological scores of animals treated with postischemic infusion of magnesium at 2h or 6h showed significant improvement ($p<0.05$). Compared to animals in control group (37.7±15.3%), magnesium treatment also caused a statistically significant decrease in infarct volume when an infusion of 90 mg/kg was initiated at 2h (14.6±11.1%, $p<0.002$) or 6h (19.7±10.2%, $p=0.008$)) but not 8h post-ischemia (30.4±13.7%, $p>0.05$). Importantly, there was no significant difference in infarct volume reduction between 2h postischemic magnesium treatment group and 4h group. These data indicate that magnesium is neuroprotective and the therapeutic window of opportunity for neuroprotection of magnesium can be extended up to 6h in focal cerebral ischemia model of this study. The apparent long window of opportunity for effective dosing may be consistent with the proposed multiple mechanisms of actions for magnesium.

P-029

Reduced Infarct Size by Systemic Application of the Free Radical Scavenger, S-PBN, 2-h after Focal Middle Cerebral Embolization in Rat.

Q. Li, Y. Yang, A. Shuaib, (Edmonton, Alberta)

Neuronal death in ischemic stroke may involve energy impairment leading to secondary excitotoxicity, and free radical generation. N-tert-butyl-(2-sulphophenyl)-nitrone (S-PBN), a free radical scavenger, has been shown to reduce oxidative stress-induced neuronal injury but rarely observed on focal cerebral ischemia model. The present study was designed to define a potential neuroprotective effect of S-PBN on focal cerebral ischemia rat subjected to right side middle cerebral artery (MCA) embolization. Wistar rats were randomly divided into two groups. Animals in control group (n=10) received vehicle and those in treatment group (n=10) were treated with intravenous infusion of S-PBN (100 mg/kg) 2h after introduction of autologous thrombus into the MCA. Percentage of cerebral infarct volumes was estimated using quantitative image analysis from 2,3,5-triphenyltetrazolieum chloride (TTC) stained coronal slices at 3 days after the ischemic insult. Neurological outcome and survival rates were also observed and compared before and after treatment or between groups. The percentage of infarct volume for animals received with vehicle was 32.8±9.4%. The percentage of infarct volume for animals receiving systemic administration of S-PBN 2h after the MCA embolization was 21.19±13% which achieved 35.4% reduction of infarct volume when comparing the control group ($p=0.017$). Moreover, infusion of S-PBN at 2h after cerebral embolization also improved neurobehavioral score. However, we have also observed that systemic application of S-PBN at a given dose in this study caused intercerebral hemorrhagical complication in 5 of 10 rats in therapeutic group (3 of 10 in control group). These data indicate that free radical generation may be involved in brain damage in this model and S-PBN may have neuroprotective effect in treatment of cerebral ischemia. Such a high incidence of cerebral hemorrhage with this agent should be drawn an attention in its future application and any possible mechanisms accounting for this complication will be further evaluated.

P-030

Postischemic Hypothermic Neuroprotection in Rat Models of Focal Cerebral Ischemia.

F. Colbourne, (Calgary, Alberta) D. Corbett, (St. John's, Newfoundland) M. Hamilton, Z. Zhao1, A.M. Buchan (Calgary, Alberta)

Background: Prolonged, but not brief, hypothermia provides long-lasting neuroprotection against global ischemia in rodents.

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Delayed hypothermia also reduces focal ischemic injury in rat, but those studies used sub-optimal durations of cooling (e.g., 3-4 hr) and short survival times (e.g., 1 day). Thus, we examined the efficacy of two days of mild hypothermia in two rat models of middle cerebral artery occlusion (MCAo).

Methods: Wistar rats were subjected to 30 min of MCAo by the intraluminal insertion of a suture combined with hypotension (60 mm Hg). Two days of hypothermia (brain temperature of 34°C) was induced 30 min into reperfusion. In the second study, spontaneously hypertensive rats were subjected to 90 min of MCAo by placement of a microclip on the MCA. Hypothermia (core temperature of 33/35°C each for 24 hr) was induced at reperfusion or 1 hr later. Infarction was quantified after a survival period of 60 (Exp. 1) or 7 days (Exp. 2).

Results: In the first study, MCAo resulted in 91% striatal loss (% contralateral side) and 36% cortical loss. Hypothermia significantly reduced striatal loss to 79% and cortical infarction to 10%. Results from the clip model will be presented at the meeting.

Conclusions: Our data are the first to prove that delayed postischemic hypothermia can significantly and persistently reduce infarction following MCAo. It is expected that similar results will be obtained in the clip model. Future work will examine if hypothermic neuroprotection translates into reduced functional deficits.

P-031

Ionizing Radiation Dose Threshold for the Elimination of Focal Epileptogenicity in the Kindled Rat

K. Elisevich, K. Jenrow, A. Ratkewicz. (Detroit, Michigan)

Rationale: Ionizing radiation diminishes epileptic expression in humans and animal models. We studied the kindling model in the rat to determine whether a threshold effect of ionizing radiation could be established in the early stages of epileptogenicity..

Methods: Male Wistar rats were kindled by electrical stimulation of the left basolateral amygdala and underwent three subsequent stage 5 seizures. Generalized seizure thresholds were determined before irradiation and thresholds established at one week intervals post irradiation. Beam collimation concentric with the electrode axis of a 6 megavolt x-ray source produced a dorsoventral exposure with a 2.5 mm radius at the 90% isodose line. Experimental groups received 10, 18, 25 and 27.5 Gy (Gray) at isocenter and compared with irradiated, nonkindled and nonirradiated, kindled controls. Animals were observed for 6 months.

Results: Seizure thresholds and durations remained unchanged following 10, 18 and 25 Gy exposures. With 27.5 Gy, 50% of rats became refractory to electrical stimulus-induced seizures and showed no electrographic abnormality beyond the stimulus artifact despite raising the current intensity to 3X the preirradiation threshold level. Rats exposed to 10 and 18 Gy showed spontaneous second convulsive episodes after the initial stimulus-induced ictus. These were of shorter duration, characterized by stage 3-5 seizures and tended to cluster towards the end of the observation period. None were observed with 25 and 27.5 Gy exposures.

Conclusion: A threshold ionizing radiation dose that eliminates kindled seizures is apparent. For rats experiencing a minimum number of stage 5 seizures, a 27.5 Gy isocenter dose approximates this effect. Double convulsive episodes reflect an enhanced excitability and manifest with lower doses (10 and 18 Gy).

P-032

A Comparison of the Effects of Barbiturates and Hypothermia on Cerebral Ischemia and Metabolism

R.L. Tyson, G.R. Sutherland (Calgary, Alberta)

Background: The effects of mild hypothermia and pentobarbital anesthesia on the metabolism of glucose and neuronal damage using a global model of ischemia were examined.

Methods: Sprague-Dawley rats were divided into three groups: two normothermic (37.5°C) groups, one under halothane and the other pentobarbital anesthesia, and one hypothermic (31.0°C) group under halothane (*N*=20 for each group). Using [1-^{13}C] glucose infused over 10, 30, 60, 100 or 200 min, the effect of hypothermia and anesthesia on cerebral metabolism was evaluated. Cerebral metabolism was arrested by freeze-funnel fixation and water-soluble metabolites were extracted from neocortex and hippocampal tissue samples with perchloric acid. Isotopic enrichments of carbon positions in glutamate, glutamine, GABA, succinate, aspartate and alanine through metabolism of [1-^{13}C]glucose were determined using nuclear magnetic resonance spectroscopy. In a separate series of experiment, the same groups of rats (*N*=9) underwent 12-min of bilateral carotid occlusion ischemia and histologically evaluated.

Results: Neuronal protection in the CA1 sector of the hippocampus was greatest in the hypothermia group, while in the neocortex both hypothermia and pentobarbital offered similar amounts of protection. Both hypothermia and pentobarbital resulted in decreased labeling of metabolites though hypothermia had a greater effect on glutamate, glutamine and GABA labeling.

Conclusions: While there are subtle differences in the effects on metabolism by hypothermia and barbiturates, hypothermia has a much greater effect in decreasing ischemic brain injury. The protective effect of hypothermia is therefore not simply through metabolic depression.

P-033

Spinal Cord Stimulation for Refractory Angina Pectoris

P.A. Pahapill, L. Schwartz, R.R. Tasker (Toronto, Ontario)

Background: Patients with refractory angina pectoris (RAP) represent an expanding population with a poor quality of life. Spinal cord stimulation (SCS) has been used extensively outside of North America for the treatment of RAP since the 1980s. SCS

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has provided patients with an increased quality of life. Use of multipolar electrodes have reduced reoperations for electrode displacement. Our goal was to provide this therapy to a small group of patients on a trial basis.

Methods: Two patients (ages 53 and 74) with RAP were entered into a pilot study. One patient had a cardiac pacemaker. Patients were assessed pre- and post-operatively with standard quality of life measures. Under local anesthesia, a quadripolar electrode with increased internodal distances (Medtronic #3888) was implanted with percutaneous techniques, approaching the C7-T1 epidural space through the T3-T4 level. Intraoperative test stimulations were performed before implantation of an ITREL-III (Medtronic) pulse generator in each patient.

Results: SCS system implantation under local anesthesia was well tolerated with a very short hospital stay in this subgroup of patients with known increased surgical risks. Preliminary results have been encouraging with significant increases in the quality of life as reflected by decreased anginal episodes, hospital visits, and dosages of nitroglycerin.

Conclusions: On the basis of our preliminary experience with SCS for RAP in a small group of patients, we conclude that SCS can be used with minimal risk and can significantly improve the quality of life in elderly patients with RAP. Patients with cardiac pacemakers remain eligible. It is probable that the use of SCS in patients with RAP will increase in North America in the new millennium.

P-034

Maintenance of TCA Cycle Kinetics in Brown-Norway Fischer 344 Rats May Translate to Longevity

R.L. Tyson, J.T. Perron, G.R. Sutherland (Calgary, Alberta)

Background: Glucose metabolism and TCA cycle kinetics has been shown to decline with age in various animal species. This study examined the relationship between TCA cycle kinetics and age in Brown-Norway Fischer 344 rats.

Methods: Using [1-^{13}C]glucose infused over 10, 30, 60 or 100 minutes, cerebral metabolism in groups of rats that were 2 (n = 18), 12 (n = 16), and 24 (n = 16) months old were evaluated. Cerebral metabolism was arrested by freeze-funnel fixation and water-soluble metabolites were extracted from neocortex and hippocampal tissue samples with perchloric acid. Isotopic enrichments of carbon positions in glutamate, glutamine, GABA, succinate, aspartate and alanine through metabolism of [1-^{13}C]glucose were determined using 1H{^{13}C} spin-echo difference nuclear magnetic resonance spectroscopy.

Results: TCA cycle kinetics did not change with age in Fischer 344 rats.

Conclusion: While other strains of rat have shown decreases in TCA cycle flux with age, the Fischer 344 rat demonstrates no age-dependent changes in cerebral metabolism. This may in part contribute to the increased longevity, minimal weight gain after 9 months of age, and decreased incidence of neoplasia in this strain.

P-035

Proteasome Inhibitor, CVT-634, Reduce Ischemic Cortical Neuronal Injury in Rats

H. Li, Z.H. Zhao, P. Sun, F. Colbourne, A.M. Buchan (Calgary, Alberta)

Introduction: Recent reports have shown that nuclear factor-κB (NF-κB) activation contributes to apoptotic neuronal death following ischemic insult. Release of the NF-κB is regulated by cytosolic proteasome. CVT-634 is proteasome inhibitor and neuroprotective in animal ischemic model. CVT-634 was tested in our transient focal ischemic model.

Method: Adult, spontaneously hypertensive rats were subjected to 90 minutes of focal cerebral ischemia by common carotid artery and right middle cerebral artery occlusion, followed by reperfusion for 22.5 hours. CVT-634 (50 mg/kg), DMSO and saline were injected i.p. at 30 minutes of ischemia and 6 hours following reperfusion. Core body temperature of the rats was maintained at 37.5 ± 0.50C during the surgery and post-ischemic period. Regional cerebral blood flows were monitored and recorded. The volume of cortical infarction was measured.

Results:

Group	Cortical Infarction (mm^3 ± SD)
Saline	118 ± 11
DMSO	108 ± 18
CVT-634	81 ± 16*

P < 0.01 (CVT-634 vs DMSO, saline)

Conclusion: The histological results suggest that proteasome and NF-κB participate in induction and regulation of apoptotic neuronal degenerative process following the transient focal ischemia of rats.

P-036

Memory in Rats with Neocortical Lesions

D. Bevzuk, T. Vorobjova, O. Bertchenko (Kharkov, Ukraine)

Limitations in the use of neurotransplantation in practical psychoneurology require research into new methodologies. The goal of the present work was to study the influence of the distant implantation of embryonic locus coeruleus (ELC) on emotional memory in rats with frontotemporal cortex lesions induced by electrocoagulation. The experiments were carried out in 18 male rats. Donor tissue was obtained from 17-18 day rat embryos and injected subcutaneously in the area of the first cervical vertebra. The model of emotional memory used was a conditional emotional avoidance reaction.

Prior to lesioning, animals were divided into two groups, one with rapid formation and one with slow formation of emotional memory. Frontotemporal cortical lesions in these animals produced an impairment of memory (inhibiting or destroying the conditional reaction stereotype) which was restored by distant implantation of ELC. In another group of rats, implantation was carried out without preceding lesioning of frontotemporal cortex.

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Effects of implantation varied according to the individual behavioural characteristics of the animals.

P-037

Neurotransplantation of Embryonic Locus Coeruleus Ameliorates Emotional Memory in Irradiated Rats

A. Goncharova, O. Bertchenko (Kharkov, Ukraine)

The effect of embryonic locus coeruleus transplantation on emotional memory was studied in 28 rats. The formation of emotional memory with the conditional emotional avoidance reaction (CEAR) and its behavioural correlates was investigated in normal rats, in rats irradiated 6 months previously (at a dose of 0.5 Gr), in falsely irradiated rats with transplantation of embryonic locus coeruleus in the frontoparietal cortex two months previously, and in rats receiving both true irradiation and transplantation.

We found that false irradiation for only a short time reduces the speed of CEAR as a result of the situational hypodynamic stress (being in the camera). In the remote period 6 months after irradiation, the stereotype of CEAR differs with stability in 86% of cases. The stereotypy of the CEAR was impaired in all rats in consequence to irradiation. Embryonic locus coeruleus transplantation in irradiated rats facilitated emotional memory. This was apparent in a reduction of organizational time of the first conditional reaction (in 96% of cases) and an increase in the quantity of CEARs in stereotype on the stage of unstable formation of emotional memory (in 80% of cases). Transplantation effects depend on the individual features of behaviour.

CEREBROVASCULAR SURGERY

P-038

Outcome and Appropriateness of Carotid Endarterectomy

M. Rodier, J. Minuk, (Montreal, Quebec)

Background: Carotid endarterectomy (CEA) is widely performed for symptomatic carotid artery stenosis and increasingly for asymptomatic stenosis. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) patient selection criteria and results remain the gold standards for symptomatic stenosis.Method: Every CEA performed during 1992-1998 at the SMBD- Jewish General Hospital in Montreal, Canada was reviewed.

Results: One hundred and eight CEA were performed on 104 patients. Vascular surgeons performed 68%, the remainder were performed by neurosurgeons. Ninety-nine of these procedures (92%) were considered to be appropriate based on the presence of recent ipsilateral symptoms in the setting of carotid stenosis >70% as determined by carotid ultrasonography and carotid arteriography. The remaining procedures were performed in asymptomatic patients or in those with cerebrovascular symptoms unrelated to the side of CEA. Of the 99 symptomatic cases, 85% were preceded by TIA, the remainder by stroke. The angiographic complication rate was 1%. Of the 99, 5 patients (5%) suffered an ipsilateral, post-operative stroke, one of which was fatal. Only 1 patient had a contralateral post-operative stroke (non-fatal). The combined stroke and mortality rate was 6.1%. Minor complications (wound hematomas/infection and cranial neuropathies) occurred in 7%. Complication rates were highest in those undergoing concomitant CEA and coronary revascularization. The incidence of post-operative complications was not related to carotid artery clamp time or shunt usage. Patch graft usage was associated with a lower post-operative complication rate.

Conclusion: The vast majority of CEA performed were considered appropriate, using NASCET criteria. TIA was the principal indication for CEA. Complication rates were acceptably low. Concomitant CEA and coronary revascularization is associated with the highest post-operative complication rate. The use of patch grafting should be considered. A permanent, ongoing database to assess the outcome of CEA has been created.

P-039

Clinical Decision Making in the Management of Patients with Ruptured Anterior Communicating Artery Aneurysm and Concurrent Carotid Artery Occlusion or Critical Stenosis.

I. G. Fleetwood and L. Cristante (Winnipeg, Manitoba)

Background: The outcome of patients with poor grade subarachnoid hemorrhage (SAH) is generally unsatisfactory. The prognosis is worse when there exists co-morbid disease that also threatens neurologic function.

Methods: We report two patients with poor grade aneurysmal SAH secondary to anterior communicating artery (ACoA) aneurysm rupture complicated by acute hydrocephalus and concomitant carotid artery stenosis (CAS). One patient was Hunt and Hess Grade IV with right internal carotid artery (ICA) occlusion. The other was Hunt and Hess Grade V with critical left ICA stenosis (99%).

Results: Management of these cases is presented. Both patients were treated conservatively and died.

Conclusions: Morbidity and mortality of poor grade SAH patients is high regardless of aneurysm location. Despite concurrent problems, it seems reasonable that patients with SAH have the aneurysm managed primarily since this is the greatest threat to life. In analyzing these cases we review aspects of ACoA aneurysm patients such as neuropsychological outcome and the specific risks of re-hemorrhage, hydrocephalus and vasospasm. Furthermore, the literature regarding issues involved in these cases such as the role of indirect surgical management, endovascular management, and management of CAS with ruptured and asymptomatic intracranial aneurysms is discussed.

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P-040

A Preliminary Report on Computerized Tomographic Angiography as an Aid to Stereotactic Radiosurgical Planning for Arterio-Venous Malformations

Brian D. Toyota (Vancouver, British Columbia)

Background: Although stereotactic radiosurgery endures as an effective means of eradicating cerebral arterio-venous malformations (AVM), there continues to be a relatively constant failure rate. A number of analyses have examined the treatment failures with a resultant list of causes. The most common cause for persistence of the lesion, despite the radiosurgery, seems to be inaccurate targeting.

Methods: We have recently begun using Computerized Tomographic Angiography (CTA) as an aid to targeting the AVM for planning purposes. Using CTA, MRI (fused) and cerebral angiography for planning purposes, six patients were treated for cerebral AVM's using a LINAC-based stereotactic radiosurgical unit. The planning process and the utility of each imaging study was reviewed.

Results/Conclusions: This presentation reports on the use of CTA as an adjunctive means of planning the radiosurgery. It will highlight and discuss the improved ability and presumed accuracy of CTA to target AVM's. It would be difficult to prospectively prove the advantage of CTA in AVM eradication (i.e. showing a higher percentage cure) because of the multiple variables which can underlie a treatment failure. However we feel the conceptual merits and case examples presented will be sufficiently persuasive for its routine use by the stereotactic radiosurgeon.

P-041

Microsurgery of Intracranial Aneurysm in Guangzhou, China: 110 Cases Report

Ren Wen-de, Qi Song-tao, Liu Cheng-yong, Ouyuang Hui (Guangzhou, China)

Introduction: Intracranial aneurysms are common in China. Microneurosurgery has been developed in many large city medical centers in past decades and presently becoming the main therapeutic intervention to deal with aneurysms. Between 1978 and 1998, we successfully operated on 110 patients with intracranial aneurysm using microsurgical techniques in our hospital. In this report, we are going to discuss our experiences of operations.

Methods: No. of cases of men and women are 61 and 49. Age range of the patients is between 20 and 63 ys, with average 48 ys. All cases were diagnosed using angiography. Among them, 58 cases subsequently underwent DSA or MRA for further assessment. All surgical operations were carried out under general anesthesia with controlled hypotension. Patients were also graded according to Hunt's classification.

Results: Aneurysms in 95 cases were successfully clipped with aneurysm body removal due to occupational effects among 15 cases and clot removal in 2 cases. Rupture of aneurysms occurred among 11 patients with only 5 patients' death.

Conclusion: Development of microsurgical techniques in our hospital has had a great impact on the efficacy of our aneurysm surgery, and dramatically reduced patient mortality.

P-042

Recognizing and Managing "Blister-like" Aneurysms of the Internal Carotid Artery

P.D. McNeely, D.B. Clarke, B. Baxter, I. Mendez (Halifax, Nova Scotia)

Background: "Blister-like" aneurysms of the supraclinoid internal carotid artery have recently been recognized as having unique pathological and clinical features. Little is known regarding their optimal treatment modality. We report, for the first time, treatment of this type of aneurysm by Guglielmi detachable coil (GDC) embolization.

Methods: Report of a case and review of the literature.

Results: A 55-year-old man presented with a Hunt & Hess grade II subarachnoid hemorrhage. Computed tomography revealed diffuse subarachnoid blood. Cerebral angiography revealed a broad based bulge on the medial wall of the right distal internal carotid artery. The patient was taken to the operating room and underwent a right pterional craniotomy and wrapping of this unclippable aneurysm. On post-operative day 11, he developed signs of vasospasm, and repeat angiography showed remarkable growth of the aneurysm. He was treated by GDC embolization of the aneurysm. On examination 3 months later, the patient was neurologically intact and angiography demonstrated obliteration of the body of the aneurysm with a very small residual neck remnant.

Conclusions: "Blister-like" aneurysms of the internal carotid artery are important to recognize and are difficult to manage using traditional surgical approaches. Early repeated cerebral angiography and endovascular therapy should be considered in the management of these patients.

P-043

CT Angiography for the Detection of Cerebral Vasospasm

Glenn B. Anderson, J. Max Findlay, Robert Ashforth. (Edmonton, Alberta)

Purpose: To prospectively compare CTA to DSA in the detection and quantification of cerebral vasospasm in the setting of acute subarachnoid hemorrhage (SAH).

Methods: Patients presenting with SAH, diagnosed on plain CT, then underwent CT angiography. Patients then underwent CTA and digital subtraction angiography (DSA) 5-10 days post bleed. All follow up CTAs were performed within 24hrs. of the DSA. The CTAs and DSAs were evaluated for vasospasm in 6 locations (ICA, M1, M2, A1, A2, basilar arteries) and graded into 4 categories (none, mild(<30%), moderate(30-50%), and

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severe(>50%)). MIP reconstructed images were used for the CTA exams, and the CTA and DSA exams were interpreted by two separate reviewers.

Results: A total of 17 patients have been studied to date. The overall agreement between CTA and DSA was 86% (Spearman correlation coefficient .830, p=.01). For proximal locations (ICA, M1, A1) the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for CTA, as compared to DSA, were 96%, 95%, 90%, 98% respectively. For distal locations (A2, M2) the sens., spec., PPV, NPV were 36%, 87%, 36%, 87%, respectively. The Spearman correlation coefficient was .921 (p=.01) for proximal and .348 (p=.01) for distal locations. In detecting none or mild spasm the sens., spec., PPV, NPV for CTA were 97%, 78%, 97%, 74%, respectively. For moderate or severe spasm the sens., spec., PPV, NPV were 78%, 97%, 74%, 97%, respectively.

Conclusions: The overall agreement between CTA and DSA in detecting vasospasm was excellent. CTA was more accurate for proximal locations than distal locations, and CTA was more sensitive for none or mild spasm but less specific than for moderate or severe spasm. In this ongoing study CTA shows promise in detecting cerebral vasospasm, but at this point cannot replace DSA in routine evaluation of patients at risk.

P-044

CT Angiography for the Detection of Carotid Artery Stenosis

Glenn B. Anderson, J. Max Findlay, Robert Ashforth, Reka Ferdinandy. (Edmonton, Alberta)

Purpose: To compare CTA with DSA for the detection of carotid artery bifurcation stenosis in patients presenting with cerebrovascular disease.

Methods: In 30 patients (60 arteries) both CTA and DSA were performed. Patients with symptomatic carotid stenosis of >50% on screening doppler ultrasound the underwent CTA and DSA. All CTAs were within 1 month of the DSA. Axial, maximum intensity projection, and shaded surface display images were produced for each CTA. The CTA and DSA exams were reviewed by two separate investigators. Measurement of stenosis was by the NASCET method and degree of stenosis was categorized also by the NASCET method.

Results: There was an overall correlation of 93% between CTA and DSA. There were 9 occlusions on DSA, these were all correctly classified by CTA. There was also perfect agreement for severe stenosis. For moderate and mild stenosis the agreement was 70% and 96%, respectively. All misclassified arteries were within one category, 3 moderate stenoses on DSA were reported as severe by CTA. One artery that was mild on DSA was reported as moderate on CTA. Accuracy for CTA compared to DSA was 94%.

Conclusions: There was a high degree (93%) of correlation between CTA and DSA for the detection of carotid stenosis. Agreement for occluded and severely stenosed arteries was perfect. There was a tendency for CTA to overestimate the degree of stenosis.

GENERAL NEUROLOGY

P-045

Evaluating the Impact of an Evidence Based Medicine Curriculum in a Neurology Training Programme

B. Demaerschalk, S. Wiebe, M. Jenkins (London, Ontario)

Background: An evidence-based medicine (EBM) curriculum was implemented at the University of Western Ontario Neurology residency. It consists of twice monthly sessions dealing with relevant neurological topics, asking focused questions, searching and appraising the evidence and applying it to individual patients.

Objective: To evaluate trainees' learning and application of EBM principles in neurology.

Methods: Using 7-point Likert scales (1=very poor/low/little, 7=very good/high/much) trainees rated the following after each session: question formulation; method, efficiency and results of literature search; validity/applicability of each article; familiarity with EBM principles; confidence in knowledge of existing evidence; ability apply evidence to practice; change in prior clinical concepts and foreseeable practice.

Results: Data are available for all (25) sessions to date. Average ratings are high/good for question formulation and literature searching (6.2, 5.9 respectively); moderate-high for familiarity with EBM principles, confidence in knowledge of existing evidence, ability to apply evidence, change in concepts and foreseeable practice (5.0, 5.7, 4.9, 4.8 respectively); moderate for article validity/applicability (4.6, 5.0 respectively). Existing literature is rated as low-moderately relevant (4.1) for individual clinical problems.

Conclusions: The EBM curriculum increases neurology trainees' confidence in knowledge of existing evidence, changes their concepts and foreseeable practice, and reinforces the EBM principles.

P-046

The Role of Trauma in the Development of Neuro Endocrineimmune System Dysregulation Syndrome

Valentin Aivazov (Pyatigorsk, Russia)

Seventy two patients with neuroendocrineimmune system dysregulation syndrome (V. Aivazov, 1998) have been studied. Twenty two of them were with consequences of cranio-cervical injury, 10 with consequences of perinatal pathology (brain hypoxia, natal trauma). Combination of consequences of the cranio-cervical injury and perinatal pathology were in 9 patients. Thus, in 41 patients the trauma was an etiological factor. There is a simultaneous suffering of the nervous, endocrine and

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immune systems (encephalopathy, goitre, diabetes, obesity, endometriosis, adenomyosis, uterine fibromyoma, mastopathy, immunodeficiency etc.), which is typical for the clinical picture of the dysregulation syndrome of III degree. Hypothalamic disorder is suggested as an anatomical basis for the syndrome.

P-047

Case Report: Thunderclap Headache as the First Symptom of Cerebral Venous Sinus Thrombosis.

A. Quirion, S. Jarjoura, (Fleurimont, Quebec), F. Evoy, (Sherbrooke, Quebec)

Thunderclap headache has been described recently as the first symptom of cerebral venous sinus thrombosis (CSVT).[1]

We report the case of a 28 year-old woman who presented with a headache of abrupt onset. Initially, the neurological examination was normal except for severe headache. The first CT-scan of the head was normal. A lumbar puncture done fourteen (14) hours after the beginning of the symptoms was normal with an opening pressure of eleven (11) cm H_2O.

Three days later, the patient developed a left sided homonymous hemianopia and a right parietal syndrome. An MRI of the brain showed a thrombosis of the superior longitudinal sinus with an abnormal signal in the right occipital lobe.

This case clearly shows that CSVT should be added to the differential diagnosis of thunderclap headache. The diagnosis of CSVT should be kept in mind despite a normal neurological exam, a normal CT-scan of the brain and a negative lumbar puncture.

1. Thunderclap headache as first symptom of cerebral venous sinus thrombosis. Lancet, 348: 1622-1625.

P-048

Human Herpes Virus (HHV)-6 Encephalitis: MRI Evidence of Reversible Bilateral Hippocampal Damage

H. MacLean, A. Douen (Ottawa, Ontario)

Background: HHV-6 is an increasingly recognized pathogen in adult immunocompromised patients and has been implicated as a cause of encephalitis. Although previous reports have suggested an affinity for the limbic system, neuroimaging has been generally unrevealing. We report a case of acute amnesia in a 20 year-old male following bone marrow transplantation.

Methods: Case Report. Investigations included neuropsychologic evaluations, serial MRIs and cerebrospinal fluid (CSF) analyses.

Results: Cognitive deficits on admission included severe anterograde as well as milder retrograde amnesia. MRI on admission revealed increased T2-signal intensity in both hippocampi. There was mild CSF pleocytosis and PCR detected the presence of HHV-6, but other viral DNA (herpes simplex, cytomegalovirus, varicella, HHV-7) was undetectable. Twelve days of I.V. acyclovir treatment resulted in improved memory but problems with encoding and consolidation were still evident. Three months after discharge, the patient's memory continued to improve and MRI showed resolution of T2 signal intensity but mild hippocampal atrophy had developed.

Conclusions: This case provides further evidence that HHV-6 can be a cause of encephalitis in adults with predilection for the limbic system. MRI can potentially aid in diagnosis. Although the natural history of HHV-6 encephalitis is not entirely clear, deaths have been reported. The clinical and radiological improvement observed following acyclovir treatment, suggests that HHV-6 encephalitis is potentially treatable.

P-049

An Examination Of Representational And Illusory Vertical Biases Using A Line Bisection Technique

S. Brennan, A. Kirk. (Saskatoon, Saskatchewan)

Background: Normal individuals may exhibit several biases when performing a line bisection task involving cues: a true vertical bias, a representational bias toward the tops of objects, and an illusionary bias toward smaller objects. Greater understanding of these directional biases could increase our knowledge of the biases operating in patients with neglect syndrome.

Methods: Thirty-six healthy, right-handed individuals each bisected 192 lines presented in four orientations: horizontal, vertical, radial down, and radial up. Four line drawings were presented at the ends of the lines, two objects that had a broad top (tree, umbrella), and two with a narrow top (mountain, bottle). Deviation of bisection mark from the midpoint of each line was measured.

Results: By collapsing across orientation, mean deviations were generated for each of the four objects. Deviations for the bottle and mountain were significantly toward the bottom of the objects. Deviations for the umbrella were significantly toward the top of the object, while deviations for the tree were not significantly different from zero.

Conclusions: A bias exists towards the broad end of objects in cued line bisection. This supports previous research, and can lead to further elucidation of the biases in both normal individuals and patients with neglect.

P-050

Primary CNS Lymphoma as a Cause of Korsakoff Syndrome

C. Toth, C. Voll (Saskatoon, Saskatchewan)

Background: Korsakoff syndrome presents with memory dysfunction with retrograde amnesia, anterograde amnesia, limited insight into dysfunction, and confabulation. The most common etiology of Korsakoff syndrome is thiamine deficiency secondary to alcoholism. There are limited case reports of structural lesions causing Korsakoff syndrome.

Methods: A 46-year-old male with a long history of alcoholism

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presented with confusion, amnesia, and confabulation with no localizing features on neurological examination. The patient showed no clinical change with intravenous thiamine.

Results: Computerized tomography (CT) of the brain revealed a heterogenous, enhancing mass lesion centered within the third ventricle, with other lesions found throughout cortical and subcortical regions. The patient was given dexamethasone intravenously without noticeable clinical improvement, but marked radiological improvement with mass reduction. Stereotactic biopsy revealed a diagnosis of Primary Central Nervous System (CNS) Lymphoma.

Conclusion: Most patients presenting with Korsakoff syndrome have thiamine deficiency, however, mass lesions can produce an identical clinical picture. This is the first case report of a patient with Primary CNS Lymphoma presenting as Korsakoff syndrome.

P-051

Wernicke's Encephalopathy Following Gastroplasty For Morbid Obesity

C. Toth, C. Voll (Saskatoon, Saskatchewan)

Background: The syndrome of Wernicke's encephalopathy consists of ataxia, ophthalmoplegia, and confusion. Predisposing risk factors include alcoholism, hyperemesis gravidarum, and prolonged intravenous feeding.

Methods: A 35-year-old female developed refractory emesis, severe weight loss, and hypokalemia following gastroplasty. Reversal of gastroplasty was performed four months following initial surgery. Following reversal, the patient developed confusion, ataxia, leg weakness, and nystagmus.

Results: Examination of the patient demonstrated disorientation with confusion, vertical nystagmus worse on downgaze, diffuse weakness of the lower extremities, and bilateral dysmetria. Magnetic Resonance Imaging demonstrated symmetrical areas of increased T2 signal present bilaterally in the medial thalamic nuclei. The patient did not demonstrate any initial improvement with intravenous thiamine. but improved over two months of follow-up.

Conclusion: Wernicke's encephalopathy has been reported in the European literature as a complication of gastroplasty, but has not previously been reported in North America. This potential complication of gastroplasty may be preventable by nutritional intervention in subjects experiencing severe weight loss and emesis following surgery.

P-052

A Variety of Migraine Visual Aura in an Artist.

A. Ogunyemi (St. John's, Newfoundland)

Background: In the last two decades, considerable progress has been made in the understanding of the mechanism of migraine headache. In contrast, knowledge about migraine aura is still enshrouded in debates and controversy. Much of the knowledge about migraine aura has been contributed by physicians and artists who have migraine. We describe an artist who suffers from a variety of migraine visual aura associated with mild unilateral headache.

Methods: The artist, a 42-year-old man, had clinical neurological evaluation by the author. EEG recording of 2 hours was obtained after overnight sleep deprivation. MRI scan of the brain was also performed. He agreed to portray in form of drawings, his aura symptoms at the time that they occur.

Results: The general medical and neurological examinations were unremarkable. The EEG and MRI scan of the brain were normal.

His drawings depicted 3 forms of migraine visual aura: (i) a pulsating bright spot which can only be seen in the dark; (ii) zigzag lines with scintillating edges which gradually migrate and diverge from the centre of field of vision to disappear in the periphery and (iii) double vision induced by intense visual concentration.

During a fourth type of visual disturbance, objects of regard or the floor would suddenly appear very close to his face. He felt as though he had lost the sense of perception for depth or distance.

Conclusion: The visual aura of migraine can be diverse and complex, even in an individual patient. The theory that will explain the mechanism of migraine aura must take the diverse manifestations into account.

P-053

Cognitive Status Assessment in Neurological Studies

S. McCrea, J.P. Das, R. Short, T. Jeerakathil, R. Ashforth, and A. Shuaib (Edmonton, Alberta)

Background: Guidelines have recently been developed for the use of cognitive tests in neurological studies. Arguments for and against the use of nonstandardized global cognitive measures in evaluating treatment effects have been advocated (Can. J. Neurol. Sci. 1995; 22: 62-71). The Das-Naglieri Cognitive Assessment System (CAS) is a standardized test of cognitive functioning that can easily be administered in under 1 hour with performance norms available from age 5 to adult.

Method: Two male patients in their early twenties with inferior and medial frontal lobe hemorrhagic contusions were assessed with the CAS at 1 week and 3 months post-injury. Patients were imaged with computed axial tomography at approximately 1 week post-injury.

Results: The CAS composite and subtest scales were sensitive to residual cognitive difficulties in planning and attention in these two patients despite them both having intact memory functions within the average to superior range.

Conclusions: Ongoing studies indicate that the CAS is sensitive to neurological injuries resulting in selective cognitive impairments, suggesting that it could potentially be useful as an efficient neurological screening, assessment or outcome measure.

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P-054

Effectiveness of Topiramate in Prophylaxis of Migraine

F. Ahmad, A. Shuaib, P. Kochanski, M. Muratoglu (Edmonton, Alberta).

Background: Topiramate is a new antiepileptic drug which was recently introduced in Canada. It has GABAergic properties which may make it an attractive prophylactic agent in migraine. In this study we evaluated the efficacy of topiramate in the treatment of migraine.

Methods: Patients with a history of migraine (with and without aura) who attended the University of Alberta Neurology Clinic were evaluated for the study. Patients with more than 6-8 migraine per month and in whom multiple other medications had not helped were approached for the study. Topiramate was used in a dose of 25-75 mg per day. Patients were followed by monthly visits.

Results: In all 30 patients were treated (24 females and 6 males) age range between 23-63 years (average 43 years). Considerable improvement was noted in 19 of 30 patients (63.3%) taking 25-75 mg of topiramate during four month of follow-up. The drug was well tolerated except for a few patients who developed minor side effects (tingling sensation and drowsiness). 11 out of 30 patients did not benefit from therapy (36.6%).

Conclusion: Our findings suggest that topiramate may be an effective drug in migraine prophylaxis. Further controlled studies in larger number of patients are needed to better evaluate its potential in migraine prophylaxis.

P-055

Saccades in Balint's Syndrome: a Quantitative Study

James A. Sharpe and Nurhan Torun. (Toronto, Ontario)

The oculomotor disorder of Balint's syndrome, "psychic paralysis of gaze", has been called "ocular motor apraxia" and "spasm of fixation". We examined these concepts by quantifying saccades in a 52-year old woman with cyclosporine induced lesions in posterior parietal areas after lung transplantation, and in four controls. Acuity and fields were normal. Horizontal saccades were recorded by magnetic search coil with: 1) predictable target steps; 2) overlap task with central target always on; 3) gap task with target off 200 msec before steps; 4)unpredictable steps; and 5) self-paced refixations. Saccadic latencies were prolonged in predictable, unpredictable and self-paced tasks ($p<0.001$). Latencies were further delayed by the overlap task and shortened by the gap task, but spasm of fixation is not a feature since gap and overlap changes, like controls, were much less than those in spasm of fixation (J Neurol Science 1992:107:603-14). Saccades were hypometric to all targets ($p<0.001$).

Ocular motor apraxia is *not* a feature of Balint's syndrome, since visually guided (reflexive) saccades were delayed like volitional predictable and self-paced saccades. Occipito-parietal disconnection from the frontal lobes can explain defective voluntary saccades to targets. Defective reflexive saccades implicate disconnection from the superior colliculi. A general defect in visual localization is consistent with damage to the dorsal, magnocellular visual pathway.

Supported by MRC of Canada Grants MT5404 and ME5509

P-056

Case Study – Neuro-recovery Six Years Post Severe Brain Trauma.

E. L. Eddy, (Winnipeg, Manitoba)

Modern techniques are enabling the survival of more brain trauma individuals. Concurrently, health care trends towards increased community integration necessitate some form of rehabilitative support in the community.

The greatest challenge is for those individuals with severe brain trauma, who survive, but are left with severe cognitive, physical and social deficits and for whom the prediction for improvement is very low, even within the two year guideline.

This case presentation describes such a situation, in which an individual has made remarkable progress six years after a motor vehicle accident. This was achieved with an individualized, consistent, intense program of rehabilitation.

The case raises several questions around issues of brain recovery beyond the two-year guideline; quality of life and who determines this; financial implications and the level of human resources required to be effective. These issues relate to professionals of all neurological disciplines, who work with such individuals.

P-057

MR Imaging with Gadolinium Enhancement for Acutely Head-injured Patients

Y. Takanashi and M. Shinonoga (Yokohama, Japan)

Background: It is critical to detect changes in the traumatic lesions before clinical deterioration in patients with early evolution of intracranial hemorrhagic lesions. The purpose of this study is to predict the development of hemorrhagic lesion(s) in head-injured patients by means of gadolinium enhanced magnetic resonance imaging (MRI).

Methods: A series of 82 head-injured patients who were admitted to emergency units presented hemorrhagic lesion(s) or not.

Results: All patients showed abnormal findings on admission CT scan. Glasgow Coma Scale (GCS) score at the time of admission in patients with gadolinium enhanced MRI was 13 or more in 13 patients , 9 to 12 in 6 patients, and 8 or less in 3 patients, respectively. 16 of 22 patients showed contrast extravasation, corresponding with evolution of lesions in size. 11 of 16 patients who had extravasation of contrast medium required surgical treatment.

Conclusions: The results of the current study may imply that extravasation of contrast medium indicates continuance of post-traumatic bleeding. MRI with gadolinium enhancement in acutely-injured patients can be a possible option for predicting the development of hemorrhagic lesions.

GENERAL NEUROSURGERY

P-058

Withdrawn

P-059

Anterior Lumbar Laparoscopic Fusion: Report of 46 cases

S. Chakravarthi, A. North, R. Anderson, J. Wellwood, R. Lemmon (Windsor, Ontario)

In 1995 we began to do BAK fusions. 45 cases have been done; 41 L5-S1 anterior laparoscopic, 1 open anterior L5-S1, 2 posterior L5-S1 and 1 posterior L4-5. The 41 L5-S1 anterior laparoscopic BAK patients are included in the study; 21 male and 20 female. Average age 44. Previous surgery 23. First surgery 18. 32 patients were interviewed retrospectively.

Patient selection for L5-S1 anterior laparoscopic BAK fusion included failure of conservative measures: back pain greater than leg pain; positive SPEC Scan at single L5-S1 level; collapse of disc space (X-ray, CT, MRI) and positive facet block.

Results: Man LOS 4d, no blood transfusions, infections, extrusions or subsidence of cages.

Complications: Retrograde ejaculation (2), Bladder perforation (1), Paralytic ileus (2).

Outcome:

Quality of Life		Narcotic Use	
Improved	21	Before surgery	23/32
Not improved	9	After surgery	13/32
Unsure	2		

Despite the low morbidity of this minimally invasive procedure patient selection remains the greatest challenge. Further assessment of screening investigations, long term follow up and comparison to posterior pedicle fusions are necessary.

P-060

Primary Management of Unstable Cervical Facet Joint Injuries with Anterior Arthrodesis

G.A. Dix and R.J. Hurlbert (Calgary, Alberta)

Background: Facet joint injury renders the cervical spine potentially unstable, invariably requiring early fusion to restore anatomical alignment and protect the cord. Posterior column instability is considered a relative contra-indication to anterior arthrodesis and, in the absence of compressive pathology or instability ventrally, posterior fusion and instrumentation are usually recommended.

Methods: We reviewed the clinical and radiographic data of 40 consecutive patients with unstable facetal injuries. All cases were treated with primary anterior cervical arthrodesis and follow-up was conducted at three and six month intervals.

Results: The procedure was well tolerated by all patients with the exception of one major post-operative complication. Six month follow-up examination revealed either immutable neurological deficits compared to pre-operative status or varying degrees of clinical improvement. Without exception, serial radiographic imaging demonstrated solid, boney union and no interim kyphosis or subluxation.

Conclusions: The efficacy of this surgical approach is enhanced by the ability to incorporate a large, solid, autologous bone mass into the arthrodesis site. Together with the relatively low complication rate, a decreased post operative pain profile and the capacity for expeditious recovery, this method is seen as an attractive option for the treatment of unstable facet joint injuries in the cervical spine.

P-061

Short Term Changes in Muscle and Bone Following Upper and Lower Motor Neuron Spinal Cord Injury – a longitudinal study of 2 adolescent males

R. Burnham, G. Bell (Edmonton, Alberta)

Background: The purpose of this study was to compare muscle and bone changes following upper and lower motor neuron paralysis early post spinal cord injury.

Methods: Two 16-year-old males were involved in the same motor vehicle accident resulting in T5 spastic paraplegia in one and T10 flaccid paraplegia in the other. Both lesions were motor and sensory complete. Vastus lateralis muscle samples were obtained by percutaneous biopsy at 2, 6, 10 and 14 weeks post injury for morphometric and quantitative histochemical analysis. Dual photon bone densitometry measurements of the legs were made 1, 2, 3, 4, and 6 months post injury.

Results: By 14 weeks post injury, the following morphometric and enzymatic changes were noted for the upper motor and (lower motor neuron) paralysed muscle: drop in type 1 fibres, 36.5% (48.7%); increase in cross sectional area, 10.2% (2.7%); myofibrillar ATPase activity, 21% decrease (3.5% increase); glyceraldehyde 3 phosphate dehydrogenase activity, 55% increase (35.5% increase); succinic dehydrogenase activity, 42% increase (40% decrease). By 6 months post injury, the subject with spastic paraplegia demonstrated a drop in bone mineral density of 15.4 and 20.0 % at the supracondylar and proximal tibia sites respectively. In comparison, the subject with flaccid paralysis demonstrated a 34.5 and 50.1% drop at the supracondylar and proximal tibia sites respectively.

Conclusions: Spinal cord injury resulted in reduction of the proportion of type 1 muscle fibres and bone mineral density

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which was most pronounced in the subject with flaccid paralysis. The muscle of the subject with flaccid paralysis also demonstrated a tendency to reduced aerobic and greater anaerobic muscle enzyme activity.

P-062

Epidermoid Cysts of the Pineal Region: A Case Report and Review of the Literature

Christopher I. MacKay, Saleh S. Baeesa, Enrique C.G. Ventureyra (Ottawa, Ontario)

Localization of epidermoid cysts to the pineal region is rare. We present a pediatric case and review 11 cases reported since 1968. Parinaud's syndrome and hydrocephalus are the most common presenting findings. Surgical treatment brought about complete resolution of the presenting symptoms and signs in 10 of the 12 cases. One patient had persistent upgaze palsy. One patient died from progression of the pineal region mass. This patient presented with hemiparesis, which should be considered a marker of clinical aggressiveness. The authors advocate direct surgical attack as opposed to stereotactic diagnosis and aspiration to: 1) decrease the likelihood of sampling error; 2) obtain maximal resection and thereby limit the potential for recurrence and delayed complications of the cyst; and 3) possibly avoid shunt placement in patients who present with hydrocephalus. These issues are felt to be of particular concern given the typically youthful ages of these patients.

P-063

Plasma Cell Granulomas of The Brain: Case report and review of the literature.

Ahmed Alkhani, Paul Muller, Sanjeev S. Deodhare (Toronto, Ontario)

Background: Plasma cell granulomas or inflammatory pseudotumors are uncommon lesions characterized by non-neoplastic proliferation of inflammatory cells mainly plasma cells. It affects the lungs in the majority of reported cases. Central Nervous System involvement is very rare where most of the cases have been described as extra-axial dural base masses. To our knowledge, only six cases of intra-axial lesions have been reported.

Method: We describe a young male who presented with a short history of intermittent headaches and a grand mal seizure. Neuroimages demonstrate a right parietal cortical mass with ring enhancement and surrounding edema. Histopathological studies revealed a plasma cells granuloma with central necrosis.

Conclusion: Primary plasma cell granuloma rarely occurs in the brain. We discuss the findings in this case with a literature review of the reported cases, and highlight the differential diagnosis and the management options of these lesions.

P-064

Perforating Tuberculous Osteitis of the Skull –Case Report

M. Hodaie, J. Bilbao, M. Muller, P. Muller (Toronto, Ontario)

Tuberculosis is endemic in many parts of the developing world and resistant forms are emerging in North America. In spite of this tuberculosis of the skull is quite rare. Tuberculosis affecting bone occurs in about 1% of cases [Davidson and Horowitz] and of these 0.2% - 1.4% have tuberculosis of the skull. Mohanty and Mukherjee reported 22 cases of tuberculosis of the skull confirmed by the presence of tubercle bacilli. They identified three types of radiological lesions –circumscribed lytic, diffuse lytic and circumscribed sclerotic. We are reporting a case of perforating skull tuberculosis that eroded the cranial vault, overlying scalp and underlying dura.

A 72-year-old female from the Philippines presented with a 3-month history of a draining open sore measuring 3 cm in diameter on the left frontal skull. She was dysphasic, right hemiparetic and obtunded. Local examination of the lesion revealed a scalp and skull defect filled with pus like material which pulsated. CT scan showed a large peripherally enhancing lesion in the frontal lobe with a thick irregular rim, perilesional edema and effacement of the lateral ventricle. The overlying bone showed complete erosion. Treatment consisted of surgical debridement, removal of what proved to be intracerebral granulation, and plastic rotation flaps to close the skin.

Histology revealed multiple necrotizing granulomatous inflammation compatible with tuberculosis and TB culture confirmed the diagnosis of mycobacterium tuberculosis. Anti - tuberculosis medication was prescribed. At 6 months post- operatively she was neurologically normal and her wound was totally healed.

P-065

Low Pressure Hydrocephalus: Two Case Reports, Review of the Literature, Pathogenesis and Treatment

Angela V. Price and Mark Hamilton, (Calgary, Alberta)

Most patients with symptomatic ventriculomegaly have high intraventricular pressures. However, there is a small subset of patients with symptomatic ventriculomegaly who have low intracranial pressure (ICP). Two such patients have been diagnosed and treated at our institution. Patient A was post-operative after posterior fossa tumor removal, the second, Patient B had TB meningo-encephalitis. Each developed clinically and radiographically significant ventriculomegaly and subsequent insertion of a ventricular catheter revealed ICP -2 to +3 cm water. The treatment instituted consisted of wrapping the patients' neck with a tensor bandage in order to indirectly increase brain turgor. This resulted in resolution of ICP abnormalities, resolution of ventriculomegaly, and significant clinical improvement. Upon removal of the neck tensor, Patient A maintained normal sized ventricles and did not require a shunt, while Patient B subsequently required venticuloperitoneal (VP) shunt insertion.

Low-pressure hydrocephalus is a little recognized entity in

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adults. The hypothesized pathophysiology is decreased brain turgor resulting in ventriculomegaly. Placing a tensor bandage around the patient's neck increases cerebral venous outflow resistance and produces a normalization of intracranial pressure dynamics and brain function.

P-066

An Alternate Theory For Abducens Nerve Palsy In Intracranial Hypertension

R. Akagami (Vancouver, British Columbia)

Background: Theories explaining abducens nerve palsies in intracranial hypertension are not satisfactory. Theories include the long intracranial length/exposure of the nerve and its vertical orientation predisposing it to injury with brainstem movement. Its intradural length is shorter than cranial nerve (CN) IV or cauda equina which are not affected by intracranial hypertension. Benign intracranial hypertension is not associated with much brainstem shift but often causes CN VI palsies. Large numbers are seen with increased intracranial pressures (ICP) but few have abducens nerve problems. A novel theory is suggested exploiting its unique intrasinus anatomy.

Methods: Theories for CN VI problems were reviewed. Cadaveric dissections were done and anatomic descriptions reviewed. 100 consecutive shunt dysfunction patients with and without Chiari II malformations were reviewed retrospectively to see if their exaggerated vertical CN orientation predisposes to CN VI palsies. Abducens palsy in low ICP situations are also discussed.

Results: The relationship of CN VI to the intracavernous carotid support the possibility of its dysfunction within the sinus. Imaging/literature support sinus compression. CN VI palsies are complications of procedures that compress the cavernous sinus area. Chiari II patients with exaggerated rostro-caudal orientation of CNs do not predispose to CN VI palsy: 2/50 Chiari II patients with a blocked shunt had a CN VI palsy vs. 2/50 patients without a Chiari II.

Conclusions: In increased ICP, it is suggested that CN VI is impinged in the cavernous sinus between the compressible lateral wall of the sinus and pulsatile carotid to which it is intimately associated. The theories for CN VI palsies remain to be proven; a case for the suggested theory is made.

P-067

Concurrent Extradural and Intradural Meningioma: A Rare Presentation of Acute Spinal Cord Compression

I. Fayaz, M. Hodaie, P.J. Muller (Toronto, Ontario)

Introduction: While spinal meningiomas are a common cause of myelopathy secondary to an intradural extramedullary tumor, extradural meningiomas, although reported in the literature, are exceedingly rare.

Case report: A 61-year-old female with a history of colon cancer presented with a 6 month history of back pain and leg numbness, with acute onset of weakness in both legs. At the time of presentation, she was ambulatory, with no bladder or bowel dysfunction. Examination revealed a T7-8 sensory level, grade 4/5 pyramidal weakness in both legs, and extensor plantar responses. An urgent myelogram/CT showed an extradural block at T6, with cord compression from T5-7. A T5-7 laminectomy was emergently performed, and gross subtotal resection of the extradural tumor achieved. Pathology revealed the tumor to be a transitional meningioma. A post-operative MRI showed circumferential dural enhancement at the level of the surgery, but no definite intradural tumor. Despite improvement in the patient's neurological status post-operatively, a re-exploration was performed. At surgery, dura with en plaque tumor was extensively resected, along with a solitary intradural meningioma, located two spinal levels higher than the extradural meningioma. The patient's post-operative course was uncomplicated, with excellent recovery of function at follow-up.

Conclusion: Though rare, meningiomas should be considered in the differential diagnosis of extradural tumors, and their presence outside the dura warrants an exploration of the intradural space.

P-068

Intrathecal Analgesia for Chronic Nonmalignant Pain. A Retrospective Review of Efficacy and Safety in 13 Patients Treated at the Kingston General Hospital

F. Espinosa, S. McKenna (Kingston, Ontario)

Background: Intrathecal administration of opioid analgesics has been used extensively for the treatment of malignant and nonmalignant pain. Overall 68.6% of patients may experience good to excellent result. We report the experience of intrathecal analgesia for nonmalignant pain in 13 patients treated at the Kingston General Hospital.

Methods: Patients were divided into 3 groups according to pain type: neuropathic, nociceptive, mixed neuropathic/nociceptive. Morphine equivalent doses were noted at monthly intervals up to 4.5 years. Pain relief was rated as poor, fair, good or excellent, at each return visit. Analgesics used included: morphine, hydromorphone, fentanyl and sufentanil with or without clonidine.

Results: Three patients failed the initial trial. This report is on the remaining 10 patients that underwent pump implantation. Overall pain relief was excellent in 60% of patients, good in 30% and fair in 10%. Two patients with neuropathic pain had excellent pain relief. Of the 5 patients with nociceptive pain, 3 (60%) had excellent relief, 1 good pain relief, and 1 patient had a fair response. Of the 3 patients with mixed pain, 1 had excellent pain relief, and 2 (66%) experienced good pain relief.

Conclusion: Long-term intrathecal administration of narcotic analgesics is efficacious, practical and safe for the treatment of most patients suffering from chronic nonmalignant pain.

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P-069

Results of Microvascular Decompression for Trigeminal Neuralgia and Hemifacial Spasm

A.M. Kaufmann, G. Olsen, T. Lye (Calgary, Alberta)

Background: The microvascular compression (MVC) disorders including trigeminal neuralgia (TN) and hemifacial spasm (HFS) typically progress in severity and extent. Literature reviews indicate that microvascular decompression (MVD) surgery offers the highest rate of cure when compared to other treatment modalities, although results may vary significantly between centers and surgeons.

Methods: A consecutive series of 136 MVD procedures were performed by the senior author between July 1996 and November 1998, including 72 for typical TN and 34 HFS. These office records were reviewed and follow-up telephone interviews conducted over a 2 to 30 month follow-up.

Results: Ages ranged from 23 to 82 years, and duration of symptoms from 1 to 23 years. All TN patients had initially responded to medical therapy but their pain had subsequently become refractory. Among HFS patients, 53% had previously received botulinum toxin injections.

Length of stay following surgery was 2 to 6 days (3.6 average). Transient post-operative complications included CSF leak treated by lumbar drain (2), self resolving pseudomeningocele (1), transient ischemic attack similar to pre-operative episodes (1), and 1 patient readmitted for aseptic meningitis without permanent sequelae. One patient suffered trochlear nerve palsy, although no patients developed deafferentation pain, *anesthesia dolarosa*, complete hearing loss, or facial palsy. There were no major surgical complications including neither death nor stroke.

Follow-up was obtained in 94% of patients at 2 to 32 months. Complete alleviation of TN and HFS was achieved in 80% and 86%, and partial symptom reduction (>75%) in an additional 12% and 4% respectively.

Conclusion: MVD can be a successful treatment for various cranial nerve MVC disorders. Surgery should be offered to patients with HFS or medically refractory TN, and be performed at specialized centers with established records of safety and effectiveness in performing MVD procedures.

P-070

Radiographic and Clinical Recovery of Subacute Stroke Following EC-IC Bypass

G.G. Vecil, A.M. Kaufmann, G.M. Klein and M.E. Hudon (Calgary, Alberta)

Background: Hemodynamic insufficiency is a rare cause of ischemic stroke. While vascular augmentation surgery has been shown to improve hemispheric cerebral blood flow, a co-operative study on EC-IC bypass anastomoses showed no clinical benefit in a large unselected patient population. However, it has been argued that a subgroup of patients may exist with physiologically definable cerebrovascular insufficiency, who may benefit from such surgery. Nevertheless, recognition of such a high risk subgroup has not been widely embraced, and there exists resistance to recommending even selective use of EC-IC bypass surgery. We report a case of a patient with hemodynamic insufficiency leading to stroke deficits and radiographic changes. Further, the patient continued to have deficits despite optimal medical therapy. We describe the process to identify his hemodynamic insufficiency, and the results of EC-IC bypass.

Methods: The patient in question presented to a peripheral hospital with signs of left hemispheric TIAs upon standing up. Investigations included CT scanning, MRI/MRA, and conventional angiography which revealed water shed territory ischemic changes. Of note the patient was found to have a spontaneous right ICA dissection with severe stenosis and a left ICA occlusion. Despite maximal medical therapy including iv heparin, hydration, and spontaneous hypertension the patient continued to have TIAs superimposed on the established unstable stroke deficit. Transcranial doppler (TCD) with diamox challenge demonstrated lack of ipsilateral cerebrovascular reserve. Therefore, the patient underwent an EC-IC bypass procedure.

Results: Following EC-IC bypass, TIA episodes stopped and the pre-operative neurological deficit abruptly improved. Furthermore, the area of cerebral injury was reduced 24 hrs following surgery compared to immediate pre-operative CT scans. Conclusions: The above findings demonstrate the existence of a patient subgroup with cerebrovascular insufficiency who may benefit from EC-IC bypass surgery. TCD diamox assessment is a readily accessible and inexpensive means to evaluate potential surgical candidates.

P-071

Diagnostic Delay In Patients With Typical Trigeminal Neuralgia

A.S. Dumont, G. Olsen, S. Verma, A.M. Kaufmann. (Calgary, Alberta)

Background: The diagnosis of trigeminal neuralgia is clinical, based largely upon a thorough history. Correct diagnosis is necessary for the initiation of effective treatment while diagnostic errors may adversely influence patient outcome.

Methods: We reviewed a consecutive series of 58 patients with typical trigeminal neuralgia who ultimately became refractory to appropriate medical therapy. Office charts and telephone interviews were employed to collect data pertaining to diagnostic history and treatment outcome.

Results: The diagnosis of trigeminal neuralgia was made in 35 +/- 14 months following symptom onset in patients receiving an initial incorrect diagnosis compared to 9 +/- 3 months in patients receiving an initial correct diagnosis ($p<0.05$). 12 patients were accurately diagnosed by the first medical professional seen, with a mean of 3.7 +/- 0.4 specialists consulted prior to diagnosis. Incorrect diagnoses included dental problems (12), temporomandibular joint (TMJ) disease (4), sinus disease (4) and migraine or cluster headache (3). The resultant interventions

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included dental procedures such as root canal or dental extraction (10), sinus surgery (2) and 1 each of TMJ surgery, Caldwell-Luc and facial cortisone injections in addition to various medications.

While all patients responded to appropriate medical treatment (eg. carbamazepine), microvascular decompression was performed when pain became refractory at 8.8 +/- 5.7 years following onset of symptoms. 86% of patients achieved an excellent or good outcome (complete relief and 75% relief of pain, respectively) at a minimum of 10 months follow-up and successful surgery was associated with initial accurate diagnosis and no prior inappropriate interventions ($p<0.05$).

Conclusions: The results from this consecutive series of 58 patients emphasize the importance of making a prompt and correct initial diagnosis to eliminate ineffective and potentially hazardous interventions in patients with typical trigeminal neuralgia.

P-072

Neurosurgical Approaches for Patients with Phantom Limb Pain

P.A. Pahapill, R.R. Tasker, A.M. Lozano (Toronto, Ontario)

Background: Phantom limb pain is difficult to treat. We assessed the efficacy of 1) dorsal column spinal cord stimulation (SCS) in 20 patients and 2) thalamic deep brain stimulation (DBS) in 4 patients with phantom limb pain.

Methods: 20 patients with phantom limb pain had a trial of SCS. Permanent implants were given to those patients with significant pain relief (>50% reduction on a visual-analogue pain scale). Four patients had thalamic DBS therapy, three of which had previous SCS therapy.

Results: SCS produced paresthesia in the phantom limb in 11 of 20 patients. Five of these 11 patients had significant pain relief at 1 month. At one year, however, only one patient continues to have relief. Two patients with appropriate SCS-induced limb paresthesia but poor pain control had similar results (good paresthesias but poor pain control) with DBS. One patient who lost paresthesia and pain control with SCS "recaptured" effective therapy with thalamic DBS. The one patient who was treated with DBS *de novo*, continues to have good pain control after 3 months.

Conclusions: Based on our results on 21 patients with phantom limb pain: 1) SCS does not provide effective therapy in the vast majority of patients, despite its relative safety and non-invasiveness; and 2) because SCS therapy is so poor for these patients, DBS therapy should be examined as a potential first-line therapy for phantom limb pain patients.

P-073

A New Method to Study the Integrity of Dural Closures

J.F. Megyesi, A. Ranger, W. McDonald and R.F. Del Maestro (London, Ontario)

Background: The watertight closure of the dura mater is fundamental to most intracranial procedures in neurosurgery. Nevertheless, for any given operator, it is still not certain which type of suture and which type of stitch affords the most watertight dural closure. In order to address these issues we have developed a laboratory model to determine the pressure at which different types of cadaveric dural closures leak.

Methods: A glass cylinder with a 6 cm opening at the top and a 2 cm port at the base is attached via a clamp to a benchtop stand. A bag of saline (infused with Evans blue for easy visualization) is attached via intravenous tubing to the port at the base of the cylinder. Pressure applied to the bag forces saline into the glass cylinder and fills it to the rim. The intravenous tubing is also Y-connected to a reservoir and, via a pressure transducer, to a chart recorder. A piece of cadaveric dura is placed over the opening at the top of the glass cylinder and secured tightly in place using a rubber O-ring. By applying force to the saline bag the dura can be stretched and the corresponding pressure recorded. An incision is made in the dura and sutured. Force is applied to the saline bag. The dural closure is visually observed for the first evidence of leakage and the corresponding pressure recorded. Using this method we have compared the closure of 3 cm dural incisions with 3-O silk using the following techniques (5 per group): 1) running, 2) running locked, 3) interrupted simple, and 4) interrupted vertical mattress. Statistical analysis was done using one-way analysis of variance (ANOVA).

Results: The mean pressures (+/- standard error of the mean) at which the dural closures leaked were: running, 15.2 +/- 2.8 mmHg; running locked, 13.7 +/- 1.0 mmHg; interrupted simple, 19.6 +/- 1.0 mmHg; interrupted vertical mattress, 14.4 +/- 2.0 mmHg. The leak pressure for interrupted simple sutures was significantly higher than for the other groups ($p<0.05$) in this small series.

Conclusions: This new method to test the integrity of dural closures should prove useful in larger and more diverse studies.

P-074

Nocardia Brain Abscess in a Non-Immunocompromised Host: Case Report and Review of the Literature

J.F. Megyesi, E. Kachur, A. Ranger and D. Steven (London, Ontario)

A 54-year-old man presented with a one month history of malaise, mild fever and cough that onset during a vacation in Florida. A chest X-ray revealed a mass in the left upper lobe of the lung which was initially thought to represent a neoplasm. The man became increasingly apathetic and then suffered a generalized seizure. Frontal lobe signs were present. A CT scan of the head revealed large bifrontal ring-enhancing lesions that encroached upon the suprasellar cistern bilaterally. Stereotactic biopsy obtained gram positive rods with beading and branching and a diagnosis of bifrontal Nocardia asteroides brain abscesses was made. Both abscesses were stereotactically aspirated for large amounts of pus and the man was placed on a triple intravenous antibiotic regimen. Despite treatment the man developed a left hemiparesis. MRI revealed a small infarction in the posterior limb

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of the right internal capsule and significant narrowing of the M1 portion of the right middle cerebral artery. Studies of the man's immune status did not reveal any abnormalities. Further treatment consisted of serial stereotactic aspirations of the abscesses. The left hemiparesis gradually improved.

A search of the medical databases revealed 96 references to Nocardia brain abscess. In the majority of these references the patients suffering with the abscesses were immunocompetent, the main reason being immunosuppression after organ transplantation. In general the organism has proven difficult to treat and clinical outcomes have been highly variable. A number of aspects of this case are different when compared to most of the other cases reported in the literature: 1) the abscesses are bilateral, large and deep, 2) the abscesses have stenosed a middle cerebral artery leading to a distal infarction, and 3) the abscesses have occurred in a non-immunocompromised patient.

P-075

Sarcoidosis Presenting as an Intramedullary Lesion of the Spinal Cord

F.B. Maroun, F.J. O'Dea, G. Mathieson, G. Murray, G. Fox, J.C. Jacob, H. Bader (St. John's, Newfoundland)

Background: Case reports of sarcoid as an intramedullary spinal cord lesion without signs of systemic sarcoidosis are exceptionally rare and it is believed that only 0.43% of patients will present in this fashion.

Methods: We presented a patient with an isolated sarcoid granuloma affecting the cervical spinal cord. History and physical data was extracted from the patient's chart. Laboratory, radiographic and pathological investigations were reviewed and presented. A literature search focusing on diagnosis and therapeutic approach was undertaken with a focus on spinal cord lesions.

Results: A 42-year-old man presented with signs and symptoms of a cervical myelopathy. A diagnosis of cervical disc disease was made and a C4/C7 laminectomy was performed with complete resolution of symptoms. Four years later he suddenly presented with quadriplegia and weakness of the right arm. MRI investigation revealed oval enhancing lesion at C5/C6. Surgical removal of the lesion was undertaken. Pathological diagnosis revealed a granulomatous lesion consistent with sarcoidosis. High dose steroid therapy was initiated. Recovery was proceeding at the time of writing.

Conclusions: Sarcoidosis affecting the spinal cord is a rare condition. It can present similarly to a neoplastic lesion and for this reason can present diagnostic and treatment difficulties. It appears that medical treatment is the mainstay of treatment. Prognosis for full recovery is guarded.

P-076

Withdrawn

P-077

Withdrawn

P-078

Fifty Years of Neurosurgery in Atlantic Canada

K. Mukhida, I. Mendez (Halifax, Nova Scotia)

September 1998 marked the occasion of the fiftieth anniversary of neurosurgery in Atlantic Canada. The Dalhousie University Division of Neurosurgery originated with the recruitment of Dr. William D. Stevenson to Halifax after he had completed his training at the University of Toronto with Dr. Kenneth G. McKenzie. Prior to Stevenson's arrival, there were no neurosurgeons in the Atlantic provinces. Minor neurosurgical procedures were carried out by a few general surgeons in Halifax, and major procedures and most elective work was referred to the Montreal Neurological Institute or the Lahey Clinic in Boston. Stevenson therefore filled a void that existed in surgical specialty service provision in Halifax.

The Division's clinical program began modestly in the late 1940s with the provision of just a few beds in the Victoria General Hospital, the largest tertiary care centre in Atlantic Canada. The opening of the Centennial Wing of the hospital in 1967 allowed the expansion of the neurosurgical unit, whose integration of radiologic, operative, and post-operative facilities made it a model for other Canadian services. Since that time, the Division of Neurosurgery has grown to include seven staff neurosurgeons and the neurosurgical unit in Saint John, New Brunswick, established in 1953, has been recently made an affiliate of the Halifax program. The division's latest move to the New Halifax Infirmary of the Queen Elizabeth II Health Sciences Centre has come with the acquisition of state-of-the-art equipment that is required in any modern tertiary care neurosurgical service in North America. The establishment of two dedicated neurosurgical research laboratories, the creation of the Clinical Research Trials Office, and the appointment of a research associate signify the division's growth and commitment to realizing Stevenson's vision of excellency in neurosurgical clinical care, education, and research in Atlantic Canada.

The past fifty years provides the opportunity not only to consider the advances and achievements that the Division of Neurosurgery has achieved, but to consider as well that such progress is the result of fifty years of work and effort by the neurosurgical team.

P-079

Fibrin-Adhesive in the Prevention of Subdural Fluid Collections following Transcortical Intraventricular and/or Paraventricular Procedures for Tumor

M. Al-Yamany and R.F. Del Maestro. (London, Ontario)

Background: Subdural fluid collections are common follow-

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ing transcortical intraventricular and/or paraventricular neurosurgical procedures for tumor. No standardized treatment for established and/or progressive subdural fluid collections which have resulted in neurological dysfunction has evolved. We have prospectively assessed the efficacy of a fibrin-adhesive (Tisseel) to close cortical and ependymal defects following intraventricular and/or paraventricular resection of tumors to prevent the development of subdural fluid collections.

Methods: From January 1994 through October 1998, twenty-five consecutive patients who underwent twenty-nine transcortical resections for intraventricular and/or paraventricular tumors were enrolled in this study.

Results: In median follow-up of 29 months (range 1 to 57 months) no symptomatic subdural fluid collections were seen. No patient developed a new seizure disorder or an exacerbation of a previous seizure problem. Seventy-two patients had pre-operative hydrocephalus and 4(22%) needed ventricular peritoneal shunting.

Conclusions: Sealing cortical and ependymal defects after transcortical procedures with a fibrin-adhesive (Tisseel) is effective in preventing subdural fluid collections.

P-080

Modified Brooks Posterior Wiring Technique With Transarticular Screws for Three-Point C1-C2 Arthrodesis

G.G. Vecil and R.J. Hurlbert (Calgary, Alberta)

Background: Many pathological conditions can contribute to instability at the atlantoaxial junction, already the most mobile region of the vertebral column. Operative C1-C2 arthrodesis is required to stabilize this segment when rigid external fixation is unlikely to result in fusion. The limitations and variable fusion rates following the traditional posterior wiring methods of Gallie and Brooks have resulted in the development of a variety of modifications that are now available to the spinal surgeon (e.g. the interspinous method of Sonntag, Halifax interlaminar clamps, and posterior transarticular screws). Of these, the transarticular screw fixation, augmented by posterior bone grafting, has become the standard of care in experienced hands. We report a novel method of posterior graft fixation to compliment screw fixation.

Methods: Our modification of Brook's technique, involves fashioning an single iliac crest graft between the posterior elements of C1 and C2. The graft is secured with bilateral multistranded sublaminar cables underneath both C1 and C2. The cables are tightened with the force directed in the natural axial direction of the spine. This construct augments internal fixation with bilateral C1/2 transarticular screws.

Results: We have used this modified Brooks wiring with transarticular screws in 11 patients between 1996-1999. To date, we have observed a 100% success rate with respect to C1-C2 fusion.

Conclusions: The modified Brooks posterior wiring for C1-C2 arthrodesis, when supplemented with transarticular screws, provides a stable construct for cervical fusion. The advantages over other techniques, lie in the axial direction of the force upon cable tightening and the ability to maintain additional stability between C2-C3 through an intact interspinous ligament. It is clearly superior to other techniques in situations where the spinous process of C2 is too acutely sloped, or small, and when the posterior arch of C1 is congenitally unfused. Improvements in pre-operative image techniques and use of multistranded cables make the potential risks of spinal cord injury negligible. In our hands the technique is both safe and efficacious.

STROKE

P-081

Morbidity and Mortality in Acute Massive Ischemic Hemispheric Infarction.

E. Isganaitis, J. Minuk (Montreal, Quebec)

Background: The outcome of acute massive ischemic hemispheric infarction (AMIHI) is generally considered to be poor. The outcome of this stroke subtype is compared with that of other stroke subtypes.

Method: Medical records of patients admitted with acute ischemic stroke to the SMBD-Jewish General Hospital in Montreal, Canada between November 1995 and January 1997 were reviewed.

Results: A total of 178 admissions for acute ischemic stroke were reviewed. Thirty-one patients (17%) were identified as suffering from AMIHI based on clinical features of the stroke; 68% of these patients died. Of those deaths, 32% occurred within 1-5 days and most were due to cerebral herniation or pneumonia. Another 26% of deaths occurred within 6-25 days. The major causes of death in this time frame were withdrawal of therapy, pneumonia and recurrent stroke. Only 32% of the patients with AMIHI survived, though most were institutionalized. In contrast, 86% of patients with non-massive ischemic stroke survived and nearly three quarters of patients were either discharged home or referred for rehabilitation. Most deaths in this group occurred within 14 days and were attributed to pulmonary sepsis or respiratory failure. For patients with AMIHI, the presence of diabetes and atrial fibrillation was associated with a 2-fold and 3.5-fold increased likelihood of death, respectively, whereas white cell count and temperature were not.

Conclusions: In this study AMIHI was associated with a significantly higher rate of mortality and dependency than non-massive acute ischemic infarction. One third of deaths in patients with AMIHI occurred within 1-5 days and were mostly attributed to cerebral herniation or pneumonia. Most survivors of AMIHI were institutionalized. The presence of diabetes or atrial fibrillation was associated with an increased likelihood of death in patients with AMIHI.

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P-082

The Interobserver Reliability of the Alberta Stroke Program Early CT Scoring System

P.A. Barber, J. Zhang, W. Hu, N. Newcommon, A.M. Buchan (Calgary, Alberta)

Background: Practical indicators which improve the selection of patients for thrombolytic stroke care are urgently needed. We developed a novel quantitative CT scan score, the Alberta Stroke Program Early CT Scoring System (ASPECTS), to predict both the risk of hemorrhage, and the functional outcome following treatment with intravenous thrombolytic therapy.

Methods: 68 consecutive pretreatment CT scans of ischaemic stroke patients treated within 3 hours with i.v. tissue-type plasminogen activator (tPa) were evaluated using the ASPECTS CT scoring system. This scoring system divides the middle cerebral artery (MCA) territory into 10 regions: 4 subcortical and 6 cortical areas. Each unaffected region receives one point. A score of zero is given to a region with early ischaemic change. A score of 10 points suggests no ischaemic change is identifiable on CT. Inter-observer variability analysis was performed for the ASPECT scoring system by two neurologists and a neuroradiologist. The scans were assessed blind to clinical information, with knowledge of the side of the stroke symptoms, and with use of a 24 hour scan.

Results: Of the 68 cases 11 scans were excluded from the analysis because of protocol violations. The percentage agreement for the absolute ASPECT scores was assessed and their respective Kappa values were calculated. The interobserver agreement was 50% (K = 0.32) for blinded scans, 50 % (K=0.37) for scans with the benefit of knowledge, and 70% (K=0.6) with the use of the 24 hour scan.

Conclusions: The ASPECT scoring system is a simple, quick and reliable to aid quantification of ischaemic change on CT in acute stroke. It can be used to help predict the risk of hemorrhage and functional outcome in the setting of acute ischaemic stroke treated with thrombolytic treatment.

P-083

Treatment of Acute Hypertension after Ischemic and Hemorrhagic Stroke: A Retrospective Review

A. Douen, C. Corman, S. Kanji (Ottawa, Ontario)

Background: Hypertension is commonly observed in acute stroke patients. Recommendations for treating post-stroke hypertension are often based on expert opinion and must be viewed cautiously. We undertook a retrospective study to (i) determine the treatment patterns of hypertension in acute ischemic and hemorrhagic stroke in a University teaching hospital, and (ii) to compare treatment patterns with guidelines based on current recommendations from the literature.

Methods: The Ottawa Hospital charts of stroke patients (109 ischemic and 23 hemorrhagic) were reviewed over a 6 month period in 1997. The use of hypertensive drugs, including dosages, routes of administration and follow up blood pressure (BP) were recorded for the first 7 days of admission.

Results: In the ischemic stroke group 39 of 109 patients had at least one reading of elevated BP. Antihypertensive medications were administered 29 times in 11 of these 39 patients. Target BP was not met 6 of 29 times and was reduced by greater than 15 percent within 24 hours 15 of 29 times. For patients with hemorrhagic stroke, 11 of the 23 patients had at least one reading of elevated BP. Acute hypertension was treated 24 times in 3 of these 11 patients. Target BP was not reached 7 of 24 times and was reduced by greater than 20 percent 8 of 24 times. Nitroglycerine paste and sublingual nifedipine were the most commonly used medications.

Conclusions: Compared to current recommendations, the choice of drugs, target BP, and BP monitoring were not optimally managed . Data from a prospective study may help to standardize patient care in this area.

P-084

Vertebral Dissection Following Golf

T. Jeerakathil, A. Shuaib (Edmonton, Alberta)

Background: There have been numerous reports of vertebral dissection following tennis, yoga, volleyball, and chiropractic manipulation. There has only been one case report in the literature of vertebral dissection following golf.

Methods: Two cases are presented of vertebral dissection following golf.

Results: A 70 year-old male had a history of one episode of paroxysmal tachycardia and left hip replacement. While playing golf, he developed difficulty with balance, mild dizziness but no vertigo. He subsequently developed diplopia and dysarthria. The symptoms subsided somewhat with only slight gait difficulty remaining. The patient was admitted to hospital. The next day the patient developed sudden left ear pain, deteriorated and required intubation. Immediate angiography was performed and revealed an occlusion of the left vertebral artery and a congenitally small right vertebral artery. Intra-arterial thrombolysis was performed with urokinase with some resolution of the clot but flow through the vessel was not restored. The patient died shortly afterwards.

A sixty-two year-old male had a history of gout and smoking but no other vascular risk factors. The patient had been on the golf course. He developed the sudden onset of left maxillary sharp pain, followed by unsteadiness and veering off to the left side. The patient was admitted to hospital and showed some improvement on the day of admission. Doppler studies revealed a left vertebral stump with no distal flow. He experienced marked improvement in his gait difficulty. The patient was discharged to a rehabilitation hospital on ASA.

Conclusions: Although no angiography was performed on the second patient, the onset of neck pain, followed by cerebellar dysfunction with an occluded vertebral artery on doppler studies is highly suggestive of vertebral dissection. The report of these two cases lends further support to the association between golf and vertebral dissection.

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P-085

Ischemic Neurological Complications in Cardiac Transplantation

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Background: Cardiac transplantation is a complicated surgical procedure and is associated with a number of neurological complications. The purpose of this study was to evaluate the cerebrovascular complication of cardiac transplantation at the University of Alberta Hospital.

Method: Information was gathered from prospective registry of all patients who had cardiac transplantation between January 1, 1985 and December 31, 1997.

Results: Two hundred and twenty orthotopic cardiac transplantation were performed on 80 patients with coronary artery disease (CAD), 109 with cardiomyopathy, 11 with congenital heart disease, 7 with rheumatic heart disease or valvular heart disease. In all 16 patients (ages 6-62 years; mean, 34 years) developed neurological complications (7.2%). These included ischemic stroke 6 of 16 (37.5 %, posterior circulation 5, carotid 1), intracerebral hemorrhage (ICH), 3 of 16 (18.75%), and encephalopathy, 7 of 16 (43.75%). The risk of stroke with orthotopic cardiac transplantation was higher in patients who had coronary artery disease or arteriosclerotic cardiovascular disease than other cardiac disease (67.7%, 4 of 6 patients). All three patients with ICH had a pre-existing risk factor for hemorrhage.

Conclusion: In our series stroke was predominantly in the posterior circulation and the presence of previous CAD increased the risk of ischemic complications.

P-086

Paradoxical Embolism Associated with Right Atrial Thrombus and Patent Foramen Ovale: Management with Intracardiac Embolectomy

M. Ursell, S. Black, G. Bhatnagar, and M. Hill (Toronto, Ontario)

Background: The role of patent foramen ovale (PFO) in cardioembolic stroke is an area of significant controversy; the diagnosis of paradoxical embolism is usually presumptive rather than proven, relying on circumstantial evidence.

Methods: We report a dramatic case of right atrial thrombus associated with PFO resulting in pulmonary emboli, splenic infarct and multiple cerebral infarcts. MRI of brain, CT angiogram of chest and intraoperative echocardiogram with be presented.

Results: A 68-year-old women presented in acute respiratory failure and coma following a seven day history of mild respiratory complaints and difficulty with vision on right lateral gaze. CT scan of the brain showed bilateral occipital infarcts. A spiral CT of the chest demonstrated bilateral pulmonary emboli. Venous Doppler ultrasound of the legs were negative for deep venous thrombosis. A transesophageal echocardiogram revealed a large, pedunculated mass in the right atrium in conjunction with a PFO. MRI of the brain four days into admission showed two new left middle cerebral artery territory infarcts suggesting ongoing embolization. She was taken to the operating room on day six and a complex thrombus adherent to PFO in the region of the coronary sinus was removed with closure of the defect. On day 30, the patient is doing neurologically well. Extensive work-up for malignancy and collagen vascular disease has been negative, however coagulopathy work-up has been positive for Lupus anticoagulant.

Conclusions: This case demonstrates proven paradoxical embolism associated with right atrial thrombus and PFO. In the rare cases where paradoxical embolism can be proven on echocardiography, intracardiac embolectomy has shown good results in our patient and in other isolated cases.

P-087

Multimedia Neurosurgery Database

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Background: There is a need for an efficient mechanism of storing clinical, imaging and operative data about neurosurgical patients that will enhance clinical audit, research, and presentations.

Methods: A computer database has been developed to record information for neurovascular surgery patents. Information recorded includes diagnoses, digitized neuroimaging studies, operation details (including intraoperative video clips), transcranial Doppler (TCD) studies, admissions and clinic visits.

Results: The database provides an audit of neurovascular cases that includes aneurysm size and location, admission grade, length of intensive care and hospital stay and outcome score. Outcome can be correlated with factors such as transcranial Doppler velocity, intraoperative blood pressure and the use of ventricular drainage, intraoperative angiography or temporary clipping. The database facilitates clinical research, allowing retrieval of patient information based on the anatomy, pathology or presentation of each clinical problem or any of the recorded intraoperative or outcome factors. The database can be used to track patients with untreated or partially treated problems such as incidental aneurysms or incompletely coiled aneurysms. The recorded images and video clips are used for teaching and producing multimedia presentations and reports.

Conclusions: A multimedia computer database has been developed that facilitates clinical audit, research and presentation activities.

NEURO-ONCOLOGY

P-088

Intracranial Melanocytoma – Report of Two Cases

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The most common pigmented tumors of the CNS are

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metastatic melanomas, which generally carry a very poor prognosis. Other pigmented intracranial tumors include meningeal melanocytoma, melanotic meningioma, pigmented schwannoma and pigmented tumors associated with cutaneous nevi. Their prognosis is very much better.

Of the 3232 surgically treated brain and spinal entries in the SMH brain tumor data bank there were 306 intracranial metastatic tumors of which 31 were melanomas [5.2%]. There were two patients who had the diagnosis of meningial melanocytoma.

One was a 63 year male who presented with a tumor associated intracranial hemorrhage. The tumor was well circumscribed an attached to the falx. Surgical resection was followed by post-operative radiation. The tumor did not recur for 10 years.

A second case is that of a 50-year-old who presented with acute cerebellar signs and was found to have a well circumscribed right cerebellar mass which was resected and irradiated. There is no suggestion of recurrence in the first post-operative year.

Meningeal melanocytomas are slow growing tumors. They may be recognized by their propensity to be dural based and have MRI characteristics that include hyperintensity on T1 with marked hypointensity on T2. The histological characteristics and immunostaining will be reviewed.

P-089

Composite Cerebellar Ganglioglioma, Pilocystic Astrocytoma, and Pleomorphic Xanthoastrocytoma: First Case Report

C.S. Haw, F. Durity, J. Maguire (Vancouver, British Columbia)

Background: Composite tumors are defined as coexistent neoplasms of different histologic type occurring in the same anatomic location. We present the first composite tumor with distinct components of ganglioglioma, pilocytic astrocytoma, and pleomorphic xanthoastrocytoma(PXA).

Methods: The patient's clinical history and radiology were reviewed. The pathological tissue was examined using light microscopic, immunohistochemical, and electron microscopic techniques.

Results: A 21-year-old woman presented with a 7 year history of headache and imbalance. Her radiological imaging revealed a partially calcified cystic lesion with two enhancing nodules in the cerebellar vermis and adjacent cerebellar hemispheres. Surgical excision was complete. Pathological examination showed the tumor to be composed of three distinct elements: ganglioglioma, pilocytic astrocytoma, and PXA. Cerebellar dysplasia was also present.

Conclusions: Composite tumors of the central nervous system have only recently been defined and are perhaps underrecognized. We present the first reported composite tumor with elements of ganglioglioma, pilocytic astrocytoma, and PXA.

P-090

Primitive neuroectodermal tumors following cranial irradiation

W.J. Hader Jr., D. Rheaume, K. Dorovini-Zis, and J.A. Maguire (Vancouver, British Columbia)

Background: Radiation induced intracranial neoplasms are uncommon but well described and include gliomas,meningiomas and sarcomas. The development of primitive neuroectodermal tumors (PNETs) following craniospinal irradiation has been reported previously only 4 times, all in children, following prophylactic irradiation and intrathecal methotrexate for acute lymphocytic leukemia and malignant lymphomas. We present four additional cases of PNETs which developed as a consequence of previous cranial irradiation.

Methods: A retrospective analysis of all patients who developed intracranial neoplasms after irradiation, from 1990-1998, at Vancouver General Hospital and British Columbia Cancer Agency, was completed.

Results: Four patients were determined to have PNETs on pathologic review. The average age at diagnosis of their initial tumors was 17 years old and the mean latency period for the second tumor was 12 years. Two PNETs were supratentorial and developed after treatment of a cerebellar ependymoma and a pilocytic astrocytoma. The other two developed in the posterior fossa following a temporal ganglioglioma and a low grade cerebellar astocytoma.

Conclusions: PNETs are an uncommon complication of cranial irradiation but should be considered in the differential diagnosis of any radiation induced neoplasm.

P-091

Hemorrhagic Surgical Complications in Malignant Brain Tumor Surgery

S. Hentschel, B. Toyota (Vancouver, Canada)

Background: For the great majority of patients with malignant brain tumors of the central nervous system (CNS) the prognosis continues to be dismal. Both quality of life and median survival are markedly limited. As such, any serious treatment complication is magnified. Hemorrhagic complications are a consistent cause of morbidity and mortality in any series dealing with the surgical care of patients with malignant CNS tumors.

Methods: We have reviewed the surgical management of patients with the diagnosis of either cerebral metastatic disease or Grade III or IV primary gliomas at the University of British Columbia since 1990.

Results: There were 604 procedures, which included 193 stereotactic biopsies, 48 open biopsies (29 via burr holes and 19 via craniotomy) and 363 craniotomies for tumor resection. Eighteen (18) hemorrhagic complications were recognized, 3% overall. There were 3 (1.6%) complications associated with stereotactic biopsies, 4 (8.3%) from open biopsies (3/29 burr hole and 1/19 craniotomy), and 11 (3.0%) secondary to craniotomies

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for resection. We have done a quantitative analysis of these complications with the intent of recognizing consistent underlying features of either the tumor's imaging appearance, patient characteristics or technical considerations.

Conclusions: Although no one feature will consistently predict a hemorrhagic complication, we will discuss features that will give the surgeon a heightened acquity for such a post-operative problem. These characteristics include the presence of a large cystic component and associated venous anomalies or draining veins.

P-092

Subacute Leukoencephalopathy Complicates Standard Early Consolidation Therapy Including Intrathecal Methotrexate

K. Wambera, J. Hukin, K. Stobart, (Vancouver, British Columbia)

Background: Methotrexate leukoencephalopathy is a well recognized complication of high dose intrathecal and intravenous methotrexate.

Methods: A 14-year-old male presented with a 24 hour history of right hemiparesis and right hemianopia following four days of headache. He had received 7 weeks of treatment for CNS negative, high risk acute lymphoblastic leukemia including a total of 48 mg (12 mg/dose) of intrathecal methotrexate and 600mg/m((75 mg/m(/dose) of intravenous cytarabine. Intrathecal methotrexate was last administered 4 days prior to presentation. He had not received craniospinal irradiation. His neurological status deteriorated over 3 days to a right hemiplegia, with right upper motor neuron facial weakness, dysarthria and left hemiataxia.

Results: A cranial MRI, at 72 hours, demonstrated bilateral frontoparietal white matter signal abnormalities suggestive of demyelination. He was diagnosed with methotrexate leukoencephalopathy and started on leucovorin treatment of 15 mg/m(/day. As there was minimal response, intravenous high dose methylprednisone was added. His neurological status improved dramatically after 48 hours to a residual mild right hemiparesis.

Conclusion: This case highlights the idiosyncratic nature of methotrexate leukoencephalopathy which can present after limited treatment with standard doses of intrathecal methotrexate and without concomitant high dose intravenous cytarabine nor craniospinal irradiation.

P-093

Activation of the Ras-MAP Kinase Signaling Pathway Correlates with Astrocytoma Grade

A. Guha, N. Lau, M. Feldkamp, (Toronto, Ontario)

Introduction: Astrocytomas do not harbor oncogenic Ras mutations, though there is a functional upregulation of this major signaling pathway carrying mitogenic signals from cell surface receptors. These published results from our laboratory was undertaken on established human malignant astrocytoma cell lines and GBMs. Here we examine whether activation of Ras and its major downstream mitogenic signaling pathway mediated by MAPKinase, correlates to grade of adult supratentorial astrocytomas.

Methods: Astrocytomas: 4-Low grade(LG), 4-Anaplastic(AA), 22-GBMs and 6-normal brain(NB) flash frozen operative specimens were analyzed by the novel enzymatic assay we have developed to measure Ras activity (Ras-GTP). Enough frozen tissue from a cohort of 11 GBMs and one normal brain were available to measure MAPKinase activity using Myelin Basic Protein (MBP) kinase assay.

Results: Ras-GTP levels in fentamoles/μg DNA: LG-1.460; AA-2.232; GBMs-2.533; NB-1.036. The normalized average MAPKinase levels was 2.523 in GBMs, which was 1.5-2.5X higher than NB. The GBMs with the highest Ras-GTP levels also had the highest MAPKinase levels.

Conclusions: This study furthers and concurs with our prior results that Ras is functionally activated in malignant human astrocytomas. Levels of Ras-GTP was increased in malignant astrocytomas (AA and GBM), correlating to increased activated receptors such as PDGF-R's and EGF-R's, in these higher grades. MAPKinase activation, the major mitogenic signaling pathway activated by Ras, was increased in GBMs in keeping with their higher proliferative index and Ras-GTP levels. These results and our prior published work suggests that inhibitors of Ras activation, which have entered clinical trials for other human cancers, may be of benefit in human malignant astrocytomas.

P-094

Expression of Activated Epidermal Growth Factor Receptors, Ras•GTP, and MAPKinase In Human Glioblastoma Multiforme Specimens.

A. Guha, M.M. Feldkamp, P. Lala, N. Lau, L. Roncari, J. Micallef, B. Salhia (Toronto, Ontario)

Introduction: Amplification of the Epidermal Growth Factor Receptor (EGF-R) is a common event in the molecular pathogenesis of high grade astrocytic tumors, occurring in 50% of glioblastoma multiforme (GBM). A subset of GBMs also expresses a constitutively phosphorylated truncated receptor (EGFRvIII). EGFRvIII has been shown to activate the Ras-MAPK pathway, and to provide a growth advantage to cells. Novel targeted chemotherapeutic agents are entering early clinical trials, necessitating means for evaluating which patients might benefit from such agents.

Methods/Results: A cohort of 12 flash-frozen operative GBM tumor specimens was evaluated for EGF-R and EGFRvIII expression and for receptor activation status using immunohistochemistry, Western blotting, and RT-PCR. Levels of activated Ras•GTP were measured using a non-radioactive luciferase-based technique. MAPK activation was determined using a myelin basic protein assay. We demonstrate a very good concordance between the specialized molecular techniques and the immunohistochemical techniques. We also demonstrate that the

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detection of either EGFRvIII or activated EGF receptors by immunohistochemistry correlates with poorer survival (EGFRvIII-positive: mean survival 4.5 ± 0.6 months; EGFRvIII-negative: mean survival 11.2 ± 0.9 months).

Conclusion: We demonstrate that easily-accessible immunohistochemical techniques are capable of determining the molecular status of GBM specimens, allowing for rapid determination of which patients may be candidates for novel molecularly-targeted agents. In addition, the characterization of specimens as to their EGF-R status appears to be of prognostic value.

P-095

Increased Expression of Vascular Endothelial Growth Factor (VEGF) by Reactive Astrocytes is Associated with Cerebral Neoangiogenesis

A. Guha, L. Angelov, B. Salhia, L. Roncari (Toronto, Ontario)

Introduction: Two components of astrogliosis in response to a variety of CNS insults includes reactive astrocytosis, and neoangiogenesis. Whether VEGF, the most potent angiogenic factor, is a common molecular link was examined.

Methods: Serial paraffin sections, representing a spectrum of CNS pathologies (N=29:trauma, abscess, infarct, alzheimers, peritumoral brain), which induce reactive astrocytosis were examined. Reactive astrocytes were identified using Ab-GFAP, blood vessels with Ab-Factor VIII, and VEGF by a polyclonal Ab-VEGF. Computer image analysis was used for quantification. The mouse (n=27) stereotactic needle CNS injury model was analyzed similarly, to evaluate the temporal relationship from days 1-9 post-injury.

Results: The degree of reactive astrocytosis, neoangiogenesis and VEGF expression were correlated, though they varied between different pathologies. Reactive astrocytes were most prominent around brain abscesses (65 /.046 mm2), expressed abundant VEGF (46% ±9% +ve VEGF signal/.046 mm2), and was associated with greatest number of vessels (??vessels/.046 mm2). In contrast, the lowest level of astrocytosis (20/.046 mm2), VEGF expression (13% ± 4% +ve VEGF signal/.046 mm2) and microvascularity (??vessels/.046 mm2) was around old traumatic gliotic scars. The mouse injury model demonstrated that the temporal expression of GFAP and VEGF by astrocytes and induced neoangiogenesis was linked, with peak expression on days 7, 6, and 5 post-injury respectively. In-situ hybridization studies are underway to determine if the VEGF positive reactive astrocytes are the source (mRNA) of the highly secreted VEGF.

Conclusions: VEGF expression is not limited to neoplastic astrocytes, but are highly expressed by benign reactive astrocytes. The expression of VEGF is linked to neoangiogenesis induced by astrogliosis, both quantitatively and temporally. Whether mitogens implicated in inducing reactive astrocytes, also induce VEGF expression is currently under study.

P-096

Development of Transgenic Mouse Models for Human Astrocytomas

A. Guha, H. Ding, S. Gertsenstein, S. MacMaster, L. Roncari, X. Wu, N. Lau, A. Nagy (Toronto, Ontario)

Introduction: Lack of a spontaneously occurring small animal model of astrocytomas is a major impediment to our detailed understanding of the molecular pathogenesis and testing of novel and conventional therapeutic agents against this currently terminal human cancer. We have used a transgenic approach to overexpress oncogenes, which our lab and others have demonstrated to be functionally relevant in human astrocytomas, specifically in astrocytes. It is hoped that expression of these transgenes will lead to a mouse model of astrocytomas.

Methods: The GFAP promoter was used to overexpress oncogenic V12-Ras; EGFR and EGFRVIII in transfected mouse embryonic stem(ES) cells, with an IRES LacZ reporter gene. The ES cells were tested for transgene expression by retinoic acid induction to turn on the GFAP promoter, and these clones were used to generate several chimaeras, from which germlines are being obtained.

Results: One strong GFAP:V12-Ras chimaera, developed GFAP positive multifocal astrocytomas 2 weeks post-natal. These tumors had a higher mitotic index, nuclear pleomorphism, increased vascularity, and higher Ras and MAPKinase activity, similar to our reported observations on human GBMs. Cell lines are currently being characterized from these tumors. Additional weaker chimaeric GFAP: Ras and GFAP:EGFR and EGFRVIII mice have led to germline transmission, which are also being characterized for later development of astrocytomas. These will also be cross-bred to knockout mice lacking in tumor suppressor genes, such as p53, p16 and Rb, postulated to be causative in human astrocytomas.

Conclusions: We have encouraging data demonstrating development of a reproducible transgenic mice model, based on our knowledge of the molecular pathogenesis of human astrocytomas. It is our belief that such models will lead to major inroads to our understanding and treatment of human astrocytomas in the future

P-097

Contribution of ERCC2 to Chloroethylnitrosourea Resistance in Human Glioma Cell Lines

Z.P. Chen, G. Mohr, L.C. Panasci. (Montreal, Quebec)

Background: We previously demonstrated a correlation between chloroethylnitrosourea (CENU) resistance and excision repair cross-complementing rodent repair deficiency gene 2 (ERCC2) expression at both the protein level (Mol Pharmacol 1997;52:815) and mRNA level (Neurosurgery 1998;42:1112) in human tumor cell lines. However, ERCC2 protein levels do not always correspond to the mRNA levels in these cell lines. Several resistant cell lines have high ERCC2 mRNA but with comparative low basal protein levels.

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Methods: In order to further clarify the rule of ERCC2 to CENU resistance in human gliomas, we treated two cell lines, in which the basal ERCC2 protein levels are similar but mRNA levels are different, with BCNU. The ERCC2 protein levels were measured at different time points after treatment.

Results: The cytotoxicities of BCNU and (2chloroethyl)-3-sarcosinamide-1-nitrosourea (SarCNU), and basal ERCC2 expression determined by both RT-PCR and Western blot analysis are listed in table. After BCNU treatment, the resistant cell line T98-G, increased its ERCC2 protein level, while the sensitive cell line SK-MG-4, did not (Fig.).

Conclusion: Our present results suggest that cell lines with high ERCC2 mRNA may be more resistant to CENUs even though their baseline ERCC2 protein levels are low. CENU treatment may induce ERCC2 protein expression in cell lines with high ERCC2 mRNA and thus contribute to resistance to these drugs.

Cell line	**Cytotoxicity (IC90, mM)**		**ERCC2**	**expression**
	BCNU	SarCNU	mRNA	Protein
T98-G	45.6	165.2	0.00074	0.065
SK-MG-4	11.0	40.6	0.000029	0.065

P-098

Adenoviral Vector Mediated Gene Transfer: Timing of Wild-Type p53 Gene Expression in Vivo and Effect of Tumour Transduction on Survival in a Rat Glioma Brachytherapy Model.

J. Bampoe, J. Glen, B. Salhia, S. Hubbard, J. Rutka, M. Bernstein (Toronto, Ontario)

Background: Optimization of the therapeutic benefit from conventional radiation therapy has stimulated investigating the enhancement of its effect on tumours. Preliminary studies indicate that wild type p53 gene (*wtp53*) expression might improve tumour kill by enabling sublethally damaged irradiated tumour cells to proceed to apoptosis.

Methods: Male F-344 rats were each given frontal 9L gliomas by stereotactic inoculation of cultured cells. 12 day old tumours were inoculated with recombinant adenoviral vectors; control rats with Ad5/RSV/GL2 (carrying the *luciferase* gene) and study rats with Ad5CMV-p53 carrying the wild type p53 gene. Brain tumours removed at specific times after transfection were measured, homogenized and lysed and *wtp*53 expression determined by Western blot analysis. Four groups of 9 rats were subsequently implanted with Iodine-125 seeds 15 days post tumour inoculation to give a minimum tumour dose of 40 or 60Gy.

Results: Wtp53 expression was maximum between days 1 and 3 after vector inoculation. 9L tumours expressing *wtp53* were smaller than *luciferase* expressing controls. This difference was not statistically significant. Radiation made a significant difference to the survival of tumour bearing rats. Moreover, *wtp53* expression conferred a significant additional survival advantage.

Conclusion: *Wtp53* expression significantly improves the survival of irradiated tumour bearing rats in our model.

The vectors in this experiment were kindly supplied by Introgen Therapeutics, Inc. Houston Tx.

P-099

Upregulation Of Uridine and Thymidine Phosphorylase In Astrocytomas

V. Sadanand (Saskatoon, Saskatchewan), A. Yusuf, J.T. Rutka, D.S.R. Sarma (Toronto, Ontario)

Cancer cells require their own blood supply during growth. As an adaptive mechanism, such cells generate various angiogenic factors which will confer survival advantage. Interestingly, many tumors upregulate Pyrimidine Nucleoside Phosphorylase (PNPase). However, this has not been reported in CNS tumors. It is well known that PNPase converts deoxyribonucleosides to 2-deoxy-D-ribose, an angiogenic factor. Thus, PNPases may play a very important role in tumor growth by aiding the development of new blood vessels.

Objective: To investigate the level of activity of PNPases in astrocytomas and to correlate this activity with tumor grade.

Methods: Varying grades of astrocytoma were used in this investigation. The post mitochondrial supernatants were used to determine PNPase activity. The enzyme preparations were incubated with either thymidine, uridine or deoxyuridine as substrates and analyzed by HPLC for PNPase breakdown products. We investigated two specific PNPases, uridine phosphorylase and thymidine phosphorylase.

Results: Higher grade astrocytomas expressed a significantly higher amount of PNPases compared to lower grades tumors. The highest level of uridine phosphorylase was in the glioblastoma multiforme while the highest level of thymidine phosphorylase was, incidentally, found to be in the gliosarcoma.

Conclusions: Preliminary results from this study suggest that PNPase activity is higher in more aggressive tumors. We propose that this may play a role in carcinogenesis through increased blood vessel formation.

P-100

B7-2/GM-CSF Combination Immunogene Therapy for Gliomas: Preliminary Results From a Pilot Clinical Trial

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Introduction: Pre-clinical studies have suggested that vaccination with irradiated autologous tumor cells transduced with the pro-inflammatory genes B7-2 and GM-CSF may be an effective treatment for malignant gliomas. We report now preliminary results from a pilot clinical trial of this therapy in recurrent glioma patients.

Methods: Two patients with recurrent gliomas received three vaccinations of 1 x 10^6 irradiated autologous tumor cells transduced with B7-2 and GM-CSF genes by the retroviral vector pLSNBG9. Patients were followed closely for signs of toxicity. Biopsy and microscopic examination of vaccination sites assessed local immune responses. ^{51}Cr-release cytotoxic T lymphocyte assays against autologous tumor assessed systemic

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immune responses. C-reactive protein levels were recorded as a measure of non-specific inflammation. Clinical course was followed with frequent examinations and imaging studies.

Results: One patient tolerated treatment well with only mild flu-like symptoms. However, the second patient developed significantly increased cerebral edema approximately three days after each vaccination. Both patients showed increased biopsy site inflammation, elevated C-reactive protein, and increased cytotoxic T cell activity against autologous tumor with each vaccination. In early follow up, clinical disease remained stable in both patients.

Conclusions: B7-2/GM-CSF immunogene therapy may induce side effects such as flu-like symptoms and increased cerebral edema in recurrent glioma patients. Vaccination appears to induce specific anti-glioma inflammatory responses. It is too early to comment on this therapy's impact on outcome, but it does not appear to be worsened in these two patients.

P-101

Prevalence of Malnutrition in Brain Tumor Patients Admitted For Tumor Resection

McCall, K. Hood, K. Rowell, R. Hanning, M. Cusimano, and P. Muller (Toronto, Ontario)

Background: The prevalence of malnutrition, while high in many forms of cancer, is unknown in the brain tumor population (malignant or benign). Significant malnutrition would justify routine nutritional screening and could affect complication rates post-operatively. This study measured the nutritional status of brain tumor patients on admission to hospital for tumor resection.

Methods: The nutritional status of patients was prospectively assessed using the Subjective Global Assessment (SGA) technique. The SGA classifies nutritional status based on changes in weight, physical exam, gastroenterologic symptoms, medical history, and changes in dietary intake and general function.

Results: Fifty-two subjects completed the study. The prevalence of malnutrition was 17%, ie. 43 were normally nourished, 7 were mildly malnourished and 2 were severely malnourished. Presence of malnutrition was not related to malignancy or symptomology (eg. headache, dysphagia). However, all malnourished patients had experienced 5 - 15% weight loss in the previous six months. Only 9% of normally nourished patients had this degree of weight loss.

Conclusions: In this first study of the prevalence of malnutrition in brain tumor patients, a low rate of malnutrition was found (17%), compared to other forms of cancer. All patients with brain tumors should be asked about weight change on admission. Referral of patients with >5% weight loss to a registered dietitian is recommended as an appropriate screening parameter to identify malnutrition.

P-102

Case Report- Acute Disseminated Intravascular Coagulation Following Meningioma Embolization

D. Yu, R. Smith, F. Espinosa (Kingston, Ontario)

Background: Preoperative embolization of meningiomas is a common adjunct to neurosurgical excision. Meningiomas are known to be associated with disorders of hemostasis perioperatively. However, cases causing surgical complications are rare. We report a case of a 78-year-old man who developed acute disseminated intravascular coagulation (DIC) during surgical excision of a large sphenoid wing meningioma which had been embolized two days prior to surgery. This case is the first to describe acute DIC following embolization of a brain tumour.

Methods: Case study.

Results: Tumour necrosis following embolization likely amplified the release of intrinsic thromboplastin and plasminogen activators at the time of surgical excision overcoming compensatory mechanisms.

Conclusions: Acute DIC following embolization of a brain tumour has never been reported. Disseminated intravascular coagulation can be life threatening and both radiologists and surgeons need to be aware of this potential complication following meningioma embolization.

P-103

The Cost of Treatment of Glioblastoma Multiforme in Nova Scotia

I. Mendez, A. MacDougall, (Halifax, Nova Scotia), Philip Jacobs (Edmonton, Alberta)

Malignant gliomas including Glioblastoma Multiforme (GBM) are the most common brain tumors in adults and account for about 2.5% of all cancer deaths. The mean survival time in individuals with GBM is 10 months irrespective of any form of therapy. Novel therapies such as local chemotherapy using implantable biodegradable polymers impregnated with BCNU (Gliadel) are currently in use in the United States and Europe and is expected to be marketed in Canada in 1999. The cost of this type of therapy could be substantial but there is no available information regarding the treatment costs of GBM using the systemic BCNU therapy in order to assess the cost effectiveness of treating the patient with Gliadel. The aim of this study was to determine the cost of treatment of GBM at our institution from the time of diagnosis to death.

A systematic chart review of 30 patients with a pathological diagnosis of GBM recently admitted to the QEII Health Sciences Centre, the only neurosurgical centre in the Province, was conducted. All medical costs incurred in treating the patient's GBM were calculated. A detailed cost analysis of diagnostic procedures, surgeries, hospital admissions as well as outpatient visits and medications was performed from the time of diagnosis to the patient's death.

Of the 30 patients in the study 58% were male and 42%

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female with a mean age of 62 years. Patients were admitted to hospital an average of 2.6 times from the time of diagnosis to their death. Survival ranged from 11 days to 26 months. Surgical procedures included stereotactic biopsies in 40% of the patients, craniotomies for tumor resection in 36% and craniotomies for resection of recurrence in 12%. Radiotherapy was given to 42% of patients and systemic chemotherapy was used in 20%.

A breakdown of costs for the different diagnostic and therapeutic modalities in these patients will be presented. The cost analysis of treating a patient with GBM will provide important information for the assessment of cost effectiveness of new therapeutic modalities such as Gliadel for the treatment of this devastating condition.

P-104

Use of Locally Implanted Chemotherapy (Gliadel) for the Treatment of Recurrent Glioblastoma Multiforme: A Report of Two Cases

S.D Christie, A. MacDougall and I. Mendez (Halifax, Nova Scotia)

Background: Current standard treatment for glioblastoma multiforme (GBM) continues to yield disappointing results. Novel approaches for the treatment of GBM are under development. One such approach is the use of biodegradable polymers impregnated with BCNU (Gliadel). Gliadel has been used as local chemotherapy in the United States and Europe and is expected to be marketed in Canada in 1999. The experience with Gliadel in two patients treated in our centre for recurrent GBM is presented. Assessment was made of the preoperative status, surgical procedure, complications and clinical outcome.

Methods: An analysis of the clinical data, imaging and pathology was conducted in two patients that presented with first recurrence of GBM. The patients were treated with surgical debulking and implantation of 8 Gliadel wafers. The patients were followed clinically and radiographically postoperatively.

Results: Two male patients, age 52 and 56 with Karnofsky scores of >90 and >80, respectively, were treated. Both patients had a previous operative removal of their GBM with postoperative radiation therapy, one of the patients was part of a gene therapy study. There were no intraoperative complications during the surgical procedure but postoperatively both patients developed significant cerebral edema in the ipsilateral hemisphere resulting in contralateral dense hemiplegia. The hemiplegia was transient in both individuals, one of the patients had complete restoration of movement approximately 10 days after the surgery, while the other improved but did not regain his preoperative status. On follow-up one patient died 8 months post-op, the other is alive with significant symptomatic tumor regrowth at 9 months.

Conclusions: Local chemotherapy using Gliadel is a novel and promising strategy for the treatment of recurrent GBM, however, the costs of the therapy and effect of complications on the quality of life of the individual patient has to be carefully balanced with the benefits of increased short term survival.

CHILD NEUROLOGY

P-105

Electroencephalographic Changes in Neonates Receiving Opiates

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Background: Opiates are commonly used in the neonatal intensive care unit (NICU). However, high dose opiates are epileptogenic in animal models and some human studies. Methods: We enrolled consecutive infants admitted to NICU if gestational age (GA)was >28 weeks, without metabolic or biochemical problems or previous seizures or neurological abnormalities. Electroencephalograms (EEGs) were done during opiate infusions and >24 hours after infusion was stopped and were interpreted blindly re: opiate administration. Results: Of 12 patients mean GA (SD) was 33.9 (± 3.6) weeks; mean birth weight was 2112.5 (773) grams. All babies had abnormal EEGs when on morphine or fentanyl. All three in whom abnormalities persisted (excessive spikes) were premature. All other EEGs off opiates were normal. The main abnormality on opiates (11 of 12) was excessive spiking; no seizures were recorded. Eight of 12 had discontinuous/invariant/nonreactive EEGs. All babies did well clinically. Conclusion: Therapeutic doses of opiates often cause EEG abnormalities in neonates; this must be considered in interpreting neonatal recordings.

P-106

The Search for Trials on Down Syndrome and 'Cognitive Enhancers'

M. S. Salman (Toronto, Ontario) S. Logan and L. Jones (London, England)

Background: Medline is a very popular and widely used source of medical information. However, the yield from Medline searches is inconsistent and varies widely among users depending on their familiarity and experience with its use. Furthermore, potentially useful information may be missed with the sole use of Medline. This study was part of a systematic review aimed at locating and critically appraising all the relevant trials where 'cognitive enhancers' were used in subjects with Down syndrome. The methods and sensitivity of the various sources used to locate the trials is presented.

Methods: Multiple search methods and highly sensitive search programs were developed to identify the relevant trials available by Dec.1996 on 9 electronic databases including Medline, EmBase, Psychological Literature, Cochrane trials register. Further sources of information were also used.

Results: 10 randomized controlled trials were identified. Medline identified the most (7 trials). Cochrane trials register and Psychological Literature identified the rest. There was an overlap in the information obtained from the various medical sources searched.

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Conclusions: Medline remains a very useful resource of medical information but it has its limitations. Hence, the need to consider additional sources of information including other electronic databases. Physicians are advised to carefully choose the right databases for their subject search and then design sensitive subject search strategies that would ensure better and more complete access to the medical information available.

P-107

Benign Myoclonic Epilepsy of Infancy: May not be so Benign at Diagnosis

M.M.S. Jan (Jeddah, Kingdom of Saudi Arabia)

Background: Benign myoclonic epilepsy of infancy (BMEI) is a rare, possibly underdiagnosed epileptic syndrome. One third of patients have family history of seizures suggesting a genetic predisposition. The clinical features are similar to that of infantile spasms, however, the development is normal and the outcome is excellent.

Method: Case description of an infant with atypical presentation of BMEI and reviewof the relevant literature.

Results: To date, 40 cases of BMEI have been described. Our infant presented at 6 months of age with a 4 week history of flexion spasms. His gestation and delivery were uneventful. His development was normal until 2 weeks into the illness when he progressively became floppy, irritable, and lost interest in external stimulation. He subsequently stopped smiling and was unable to sit with support. EEG, brain MRI, and detailed metabolic work-up were normal. Vigabatrin resulted in complete seizure control. Detailed follow-up assessment at 10, 12, and 18 months revealed normal development with no seizures.

Conclusions: Developmental regression could occur in BMEI if the seizures are not treated early, however, the prognosis remain favorable. Mislabeling these infants as infantile spasms may explain why a few infants in many of the infantile spasms series have an excellent outcome.

P-108

Systemic Functional Aspects of Rehabilitation in Children with Organic Injuries of the Nervous System

V. Martyniuk (Kiev, Ukraine)

Rehabilitation of children with organic nervous system injuries requires the integration of multiple disciplines including medical, psychological, pedagogical and socially-therapeutic. A systemic approach to this rehabilitation is required, restoring function while taking into account individual peculiarities of the child in general, including the development and injury of the nervous system.

In order to individualize rehabilitation programs, the following 4 main functional systems are recognized: 1) the functional system of motion (from an initial reflectory motion to a conscious voluntary action); 2) the sensory functional system (from sensibility and elementary senses to perception, including social); 3) the functional system of cognition and speech (from word recognition and elementary speech signals to the formation of higher cognitive activity and speech); and 4) the functional system of emotion and personality (from elementary emotionally communicative reactions to motivation and personal adaptations to the social environment).

Rehabilitation in terms of these functional systems is complex, requiring the cooperation of multiple specialists and of the child's parents.

P-109

Post-Varicella Angiopathy - Report Of A Case With Pathological Correlation.

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Background: Varicella is a common childhood illness. Complications of the central nervous system are second only to cutaneous complications. Delayed angiopathy has been described, although few reports exist within the pediatric literature with clinico-pathological correlation.

Methods: We report a previously well 4-year-old boy who had an episode of varicella two months prior to admission with skin lesions most marked on the right side of his face and neck. He presented with massive right middle cerebral artery (M.C.A.) infarction. At 72 hours he developed cerebral oedema refractory to treatment with mannitol and hyperventilation and transtentorial herniation. Right frontal temporoparietal craniotomies were performed on two occasions over the subsequent 24 hours, with evacuation of infarcted brain tissue.

Results: Cerebral angiography 48 hours post onset demonstrated an isolated 90% stenosis of the right proximal M.C.A. Laboratory investigations, including coagulation studies and tests for hypercoagulability, and echocardiography were all normal. Light microscopy, immunohistochemistry and electron microscopy, were performed on the surgical specimens. Some intraparenchymal small vessels showed vasculitis with lymphocytes in the cell wall. Areas of demyelination were present within the white matter.

Conclusion: Delayed angiopathy, whilst an uncommon complication of varicella, may affect both small and large blood vessels, with catastrophic results.

P-110

Progressive Facial Hemiatrophy: An Unusual Craniofacial Dysgenesis

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Background: Progressive facial hemiatrophy (Parry Romberg syndrome) presents in childhood with progressive, focal facial atrophy. Neurological problems include epilepsy and cerebral structural abnormalities.

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Methods: At 2 years of age, this girl was noted to have a mild, nonprogressive left hemiparesis. Progressive atrophy of the right facial structures occurred despite treatment with methotrexate and prednisone. Her academic performance is normal and she has not had seizures. The birth history was normal. There is no family history of connective tissue disorders.

Results: Serial cranial CT scans, at 7 and 9 years of age demonstrated nonprogressive calcification in the right basal ganglia and blurred grey/white matter interface in the right hemisphere. The right maxilla was small. MRI demonstrated abnormal thick, irregular right frontal and parietal grey matter ("pachygyria"), focal dilation of the right lateral ventricle lined by abnormal grey matter ("closed lip schizencephaly") and atrophy of the right cerebellum. Investigations for collagen vascular diseases were normal.

Conclusion: These observations suggest that the progressive facial hemiatrophy results from cerebral dysgenesis involving the rostral neural plate which becomes more visible during the time of cephalic growth.

P-111

Acute Disseminated Encephalomyelitis – Possible Evolution

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Background: Acute disseminated encephalomyelitis (ADEM) is a demyelinating disorder of the CNS which appears to be immune mediated. Demyelination is best seen by MRI. We present a young girl whose initial presentation did not suggest ADEM and wonder if we witnessed the evolution of this disorder.

Case Description: Over a four week period, this previously well 8 9/12-year-old aboriginal girl developed increasingly severe headaches, focal seizures, lethargy and eventually apneic spells requiring ventilatory support. She had papilledema, a normal CT, elevated intracranial pressure and a CSF cell count of 67 (predominantly mononuclear cells). Her MRI showed mainly diffuse pial enhancement of the cerebral hemispheres consistent with meningitis. A biopsy of cerebral cortex showed numerous lymphocytes and occasional polymorphonuclear leukocytes in the arachnoid indicative of acute meningoencephalitis. No specific viral features were identified. She recovered rapidly on mannitol and high dose steroids but developed acute unilateral optic neuritis on rapid steroid taper. She improved quickly with resumption of high dose steroids and then remained relatively asymptomatic on gradually tapering steroids for 7 months. She recurred two months after steroid discontinuation. A repeat MRI showed extensive areas of increased signal intensity on T2 weighted images in the white matter of cerebral hemispheres, brain stem and cerebellum. A second biopsy showed chronic perivenous inflammation, gliosis and mild focal myelin loss. Her clinical status and MRI findings improved with steroids. She has remained stable for eight months with steroid tapering and monthly infusions of intravenous gamma globulin (IVIG).

Conclusions: Our presumptive diagnosis is ADEM on the basis of her recurrent encephalopathy with extensive white matter lesions and her apparent response to steroids. We wonder if a picture of meningoencephalitis can precede the development of white matter abnormalities in ADEM, making initial diagnosis difficult. Finally, while we cannot be certain in this case, IVIG may offer adjunctive perhaps steroid-sparing treatment.

P-112

Landau-Kleffner Syndrome (LKS) : A discrete neuropathologic substrate?

W. Ziai, H. Darwish, L. Alfaro, V. Lange (Calgary, Alberta)

Background: The cases of LKS documented in the literature represent a spectrum of abnormalities.

Objective: We report a case of childhood acquired aphasia with seizures and analyze the course and electrophysiologic abnormalities to define specificity of LKS.

Method: Case report with serial electrophysiologic studies and correlation with language and motor abilities.

Results:

Presentation: Subacute onset of expressive and auditory receptive language dysfunction with focal motor seizure activity (of right mouth and hand). Mild motor weakness and incoordination of right hand and complete astereognosis were present.

Clinical Course: Gradual sequential improvement of seizures, followed in order by speech, motor control and lastly astereognosis. Relevant studies: EEG showed left central and mid parietal sharp transients and slow waves. SEPs initially showed no responses from right median nerve. This recovered, but abnormal responses from right posterior tibial nerve persisted. Neuroimaging (MRI) and CSF studies were unremarkable.

Discussion: 1. The sequence of clinical recovery is notable for the sustained abnormality of the posterior tibial SEP long after recovery of language. 2. The EEG in sleep did not show CSWS. 3. Clobazam controlled the seizures but language improvement started only after flunarazine was added. Was language recovery spontaneous? 4. This is the first time SEP studies have been reported which show a much more widespread involvement than previously documented.

Conclusion: The findings support the concept that LKS as reported is not a homogenous entity and does not have a distinct neurologic impairment. The SEP changes define a wider area of disturbance than previously considered. The pathophysiology is still unclear.

P-113

The Application of the Multiattribute Health Status Classification (MAHSC) to 3- through 17-Year-Old Survivors of Pediatric Intensive Care (PIC) Treated For Severe Closed Head Injury (CHI) and Hypoxic-Ischemic Encephalopathy (HIE)

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Background: A single, valid and reliable outcome measure is

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needed for surviving children receiving PIC for severe CHI/HIE. The tool should provide levels of functioning in areas important to well being, be capable of completion by parents/guardians, and accurately reflect the full range of possible outcomes. It could be used for individual prognostic counselling, as an outcome measure for future therapeutic trials, and as a screening tool to ensure children in need of intervention are enrolled in programs. The MAHSC has been used for survivors of childhood cancer, extreme prematurity, and PIC.

Methods: Two studies address this: (1) An interrater reliability (parent, 2 physicians) study of the MAHSC attributes of sensation, mobility, emotion, cognition, self-care, pain, behaviour, and general health, was carried out for 50 patients ages 5 to 18 years from the Pediatric Brain Injury Program. (2) A parental MAHSC was completed 6 months after severe CHI/HIE with Glasgow Coma Scores (GCS) 8 or intubation for focal neurologic findings or airway protection attributable to HIE (n=52) (ages 4-18 years) and results compared with 2 to 5 on the Glasgow Outcome Scale (GOS). Step-wise multiple regressions determined which early predictive variables contributed to adverse outcome.

Results: (1) Significant (0.01) agreement (i.e. 70%) was found between parents and physicians for all attributes but pain, where agreement was 60%. (2) 39 of 52 children had a good recovery on the GOS, yet 20 of these 39 had abnormal attributes on the MAHSC. Only 9 of 52 children had an entirely normal MAHSC. 53% of the variance for abnormal GOS was determined by more doses of epinephrine, more days to sustained eye opening, lower age at insult, lower GCS. 46% of the variance of abnormal MAHSC was determined by more doses of epinephrine, lower GCS, lower arterial pH, other head trauma.

Conclusion: The MAHSC should be broadly accepted as an outcome measure for children following severe CHI/HIE.

P-114

Migraine after Childhood Ischemic Stroke: Cause or Sequela?

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Objective: To examine the prevalence of migraine in children after stroke and to analyze migraine occurring in post stroke patients particularly in those with no pre stroke history of migraine.

Design/Methods: In a retrospective single cohort study, 75 pediatric post stroke patients were reviewed using data from the Neurological Stroke Registry Outcome clinical assessment forms. A descriptive analysis of those patients who had migraine post stroke and not pre stroke was examined (age, sex, neurological risk factors, including varicella, head injury and family history of migraine). Using the International Headache Society criteria, patients with migraine were then analysed from the sample of patients who experienced any headache at all post stroke, including the infarct characteristics, etiology if determined and the neurological outcome (sensorimotor skills, language production and comprehension, and cognition).

Results: In this sample, 15% of children had migraine after stroke: 4% of children were between 0-7yrs, 8% were between 7-15yrs and 2.5% were 15yrs plus. 10% of patients had no pre stroke migraine but did have post stroke migraine.Only 1% of patients had pre stroke migraine and not post stroke migraine.There were a greater number of males who experienced post stroke migraine without a pre stroke history (62.5%). Most of the children who experienced migraine with no prestroke migraine were between 5-10yrs. Due to the small sample size of the neurological risk factors no statistical significance may be concluded, however, 62.5% had chicken pox prior to the stroke onset, 18.75% had had prior head injury and 12.5% has a family history of migraine.Supporting the hypothesis that migraine occurred as a result of a stroke, 87% of the sample had no risk factors for the development of migraine. 21.3% of post stroke children experienced undefined headaches.

Conclusions: This data demonstrates that there is a 15% prevalence of children who experience migraine post stroke with no pre stroke history of migraine.This data would suggest there is an increased prevalence of migraine after stroke compared to the 4-5% of the general pediatric migraine population.Stroke may be a causative factor in the development of post stroke migraines in children.

P-115

Neurodevelopmental Outcome of Young Pediatric Intensive Care (PIC) Survivors of Serious Brain Injury: A Preliminary Report.

C.M.T. Robertson, M-J. Watt, A.R. Joffe, D.E. McLean A.J. Moore, K.S. Pain (Edmonton, Alberta)

Background: Updated knowledge on the outcome of children of 3 years that require PIC for closed head injury (CHI) or hypoxic-ischemic encephalopathy (HIE) is needed to improve individual prognostic counselling and as a background for trials of new interventions.

Methods: All children of 3 years of age at the time of admission to PIC of Northern Alberta for CHI or HIE from 1995 to 1997 were recruited. Entry criteria included Glasgow Coma Score 8 or intubation for focal neurologic findings or airway protection attributed to HIE. Children with pre-insult Central Nervous System malformation, cerebral palsy, chromosomal abnormality or primary heart disease were excluded. Survivors received multidisciplinary assessment from 18 to 38 months of age, at least 6 months after PIC discharge at the Neonatal and Infant Follow-up Clinic, Glenrose Rehabilitation Hospital.

Results: 45 subjects made up 5% of all PIC admissions 3 years of age. Mean age at admission 9.5 (range 1-32) months. 10 died, and 4 were lost to follow-up. Of the surviving 31 assessed children, 17 (55%) had Bayley Scales of Infant Development, Mental Developmental Indices of 70, with or without associated neuromotor disability. Only 4 assessed survivors had Mental and Motor indices within the average range (85).

Conclusion: In addition to a focus on prevention, new neuroprotective treatments for brain injury are urgently needed for these high-risk children.

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NEUROMUSCULAR DISEASE

P-116

Myotubular Myopathy with Cardiomyopathy Requiring Heart Transplant

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Background: Myotubular myopathy has been extremely rarely associated with cardiomyopathy, which can lead to heart failure and premature death.

Methods - Case Report: A 3 1/2-year-old girl presented with a rapid onset dilated cardiomyopathy, biventricular hypertrophy and mild proximal muscle weakness in conjunction with histologic features consistent with myotubular myopathy. After unsuccessful medical treatment for heart failure, the girl underwent orthotopic cardiac transplantation at the age of 4 1/2 years. Currently, one year after the heart transplant, there are no signs of rejection.

Results: Skeletal muscle biopsy showed increased central nuclei and perinuclear vacuolation and aggregates of mitochondria. Examination of the heart at the time of transplantation confirmed a dilated cardiomyopathy. Histology revealed hypertrophic myocardiocytes, focal areas of infarction, and endocardial fibroelastosis.

Conclusions: Although cardiomyopathy is commonly associated with other childhood myopathies, it is rare in myotubular myopathy. Our patient is the youngest case of myotubular myopathy presenting with heart failure and the first case that successfully underwent cardiac transplantation. We recommend detailed cardiac assessment with regular follow-ups in children with histologic features consistent with myotubular myopathy.

P-117

Lumbosacral Plexopathy following Ovarian Hyper-Stimulation Syndrome

R. Leckey, T.J. Benstead, I.A. Grant (Halifax, Nova Scotia)

Background: Ovarian hyperstimulation syndrome (OHS) is an uncommon complication of proovulatory agents for treatment of infertility. We report the case of a 34-year-old female who developed a right lumbosacral plexopathy following severe OHS, a previously unreported complication.

Methods: A 34-year-old female was assessed 6 weeks after developing OHS. During the illness she developed moderate azotemia, marked lower extremity edema, ascites and the ovaries enlarged to 10-12 cm by ultrasound. After diuresis she noted a right foot drop. During hospitalization there were no IM gluteal injections or periods of immobility. There was no previous neurologic history. There was no pain except for dysesthesia of the great toe. Examination demonstrated grade 3/5 dorsiflexion, inversion and eversion of the right ankle and grade 4/5 toe flexion. There was absent sensation in the lower leg laterally. All other muscle groups had normal power and all reflexes were normal.

Results: Nerve conduction studies on the right revealed markedly reduced peroneal compound muscle action potential amplitude. Tibial motor conduction, F-wave and H-reflex were normal. Sural response was reduced and superficial peroneal response was absent, but normal on the left side. Needle EMG revealed fibrillations in the tibialis anterior, tibialis posterior, tensor fascia lata and gluteus maximus. Medial gastrocnemius showed decreased recruitment and polyphasic motor unit potentials as did the above muscles. Low-lumbar paraspinals and vastus medialis were normal.

Conclusion: The patient developed a right L5-S1 lumbosacral plexopathy, presumably compressive, related to intra-abdominal fluid or enlarged ovaries. In a medline search of 1986-1998 there have been no reports of lumbosacral plexopathy after OHS. This complication may become more frequent as the use of proovulatory agents increases.

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