35th MEETING OF THE CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES

JUNE 13- 17, 2000
OTTAWA, ONTARIO

PROGRAM AND ABSTRACTS

TUESDAY JUNE 13, 2000

NEUROBIOLOGY REVIEW COURSE

Chairs: Garth Bray, Vincent Castellucci

Presentation I: Ion Channels and Membrane Excitability General Principles
Ion channels and peripheral nerve disorders ..... *Michael Rasminsky (Montreal, QC)*
Ion channels and muscle disease .. *George Karpati (Montreal, QC)*

Presentation II: Cell Death and Neurologic Disease
Basic mechanisms of cell death .... *Freda Miller (Montreal, QC)*
Spinal muscular atrophy: Neuron death due to mutations of specific genes ..... *Alex MacKenzie (Ottawa, ON)*

Presentation III: Cerebral Ischemia
Pathophysiology ..... *Antoine Hakim (Ottawa, ON)*
Rationale for surgical treatment ..... *Max Findlay (London, ON)*

Presentation IV: Movement Disorders: Physiology and Pharmacology
Pharmacology..... *David A. Grimes (Ottawa, ON)*
Rationale for surgical intervention ..... *Zelma Kiss (Ottawa, ON)*

2ND ANNUAL ALS STRATEGIES FOR QUALITY LIFE/QUALITY CARE

Chairs: Michael Strong, Suzanne Lawson

What is ALS? ..... *Marek Gawel (Toronto, ON)*
Advances in respiratory intervention ..... *Douglas McKim (Ottawa, ON)*
Advances in dietary intervention *Rup Tandan (Burlington, USA)*
Panel: **Getting help in the Ottawa Region.**
Who? Where? When?
What the ALS Society does..... *Richard Woods (ALS Society of Ontario) (Ottawa, ON),*
..... *Karen Omerod, (Ottawa, ON),*
..... *Suzanne Lawson (Toronto, ON),*
Home Care, Respirology Service, Home Occupational Therapy
Panel: **Coping with the challenges of ALS**
..... *Chair: Angela Genge (Montreal, QC)PALS, Caregivers, Health Care Providers*
Breakout session: Advanced directives, Dental management, Respiratory management, Meet the Experts
The future in ALS:
A research update ..... *Michael Strong (London, ON)*

EPILEPSY VIDEO SESSION

Chair: Richard McLachlan

Seizures in adults ..... *Michael Jones (Vancouver, BC)*
Seizures in children ..... *TBA*
More seizures ..... *Richard Desbiens (Quebec City, QC)*
Rabbit seizures..... *Richard McLachlan (London, ON)*

VASCULAR DEMENTIA

Chair: Sandra Black

From multi-infarct dementia to vascular cognitive impairment: historical perspective and new directions ..... *Vladimir Hachinski (London, ON)*
Diagnostic criteria, co-morbidity with other dementia and epidemiology: a Canadian perspective from the civic study..... *Kenneth Rockwood (Halifax, NS)*
Quantifying the ABCs of the dementia syndrome: atrophy, behaviour, and cerebrovascular diseases ..... *Sandra Black (Toronto, ON)*

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WEDNESDAY JUNE 14, 2000

MANAGEMENT OF DISORDERS OF THE CRANIOCERVICAL JUNCTION

Chair: Michael Fehlings

Anatomy biomechanics craniocervical junction ..... *John Hurlbert (Calgary, AB)*
Management of osseous pathology at the craniocervical junction ..... *Michael Fehlings (Toronto, ON)*
Hands on session ..... *Faculty*
Management of tumours of the craniocervical junction ..... *Fred Gentili (Toronto, ON)*
Chiari malformation ..... *Charles Tator (Toronto, ON)*

MEDICAL MALPRACTICE AND THE PEDIATRIC NEUROLOGIST: LEGAL AND MEDICAL PERSPECTIVES

Chair: Michael Shevell

Medical malpractice – A defendant counsel's perspective ..... *Charles Hackland (Ottawa, ON)*
Medical malpractice – A plaintiff counsel's perspective ..... *Peter Hagen (Ottawa, ON)*
Medical malpractice and pediatric neurology ..... *Anne Cornet, MD (Ottawa, ON)*
The pediatric neurologists as expert witness ..... *Michael Shevell, MD (Montreal, QC)*

MOLECULAR MECHANISMS OF EPILEPTIC SYNDROMES

Chairs: Monique D'Amour, Alan Guberman

Genetics of epilepsy ..... *Eva Andermann (Montreal, QC)*
Molecular mechanisms of primary generalized epilepsies .. *Philip Schwartzkroin (Seattle, USA)*
EEG characteristics of primary generalized epilepsies ..... *Warren Blume (London, ON)*
EEG characteristics of hereditary focal epilepsies ..... *Fred Andermann (Montreal, QC)*
Molecular mechanisms of antiepileptic drugs ..... *Jack Schneiderman (Toronto, ON)*

EVIDENCE-BASED NEUROLOGY

Chair: Sam Wiebe

Principles of evidence based neurology ..... *Samuel Wiebe (London, ON)*
CAT walk (What is a CAT?) . *Bart Demaerschalk (London, ON)*
Workshop: Asking answerable questions and finding the evidence ... *Samuel Wiebe, Bart Demaerschalk (London, ON)*
Workshop: Appraising the evidence ..... *Samuel Wiebe, Bart Demaerschalk (London, ON)*
Workshop: Applying the evidence ..... *Samuel Wiebe, Bart Demaerschalk (London, ON)*

CURRENT EDUCATIONAL ISSUES IN THE CLINICAL NEUROSCIENCES

Chair: J. Max Findlay
Resident associations and training: Past, present, and future ..... *Derek Puddester, (Past President of the Canadian Association of Interns and Residents) (Ottawa, ON)*
The development of standards for resident training program accreditation ..... *Nadia Z. Mikhael (RCPSC Director of Education) (Ottawa, ON)*
Resident training program evaluation (and what is behind an excellent program) ..... *George Goldsand (Former Associate Dean Post-Graduate of Medical Education, University of Alberta) (Edmonton, AB)*

Chair: Chris Wallace
Perspectives from program directors: The delicate service to education balance
English Neurology Programs .... *George Elleker (Edmonton, AB)*
English Neurosurgery Programs .. *Brian Toyota (Vancouver, BC)*
French Neurology Programs ..... *Richard Desbiens (Laval, QC)*
French Neurosurgery Programs *Philippe Couillard (Sherbrooke, QC)*
Manpower needs in the neurosciences ..... *Herman Hugenholtz (Halifax, NS)*

MOLECULAR MECHANISMS OF NEUROMUSCULAR DISEASE

Chair: George Elleker

The muscular dystrophies: phenotypy, genotypy and the molecular biology of muscle .... *Michael Brooke (Edmonton, AB)*
The channelopathies ..... *Dennis Bulman (Ottawa, ON)*
The spinal muscular atrophies .... *Alex MacKenzie (Ottawa, ON)*
Hereditary neuropathies: phenotypy and genotypy ..... *Angelika Hahn (London, ON)*
Antibody – mediated neuropathies ... *Tom Feasby (Calgary AB)*

CASE HISTORIES IN NEUROCRITICAL CARE

Chair: Jeanne Teitelbaum

A massive stroke, with medical complications ..... *Jeanne Teitelbaum(Montreal, QC)*
Myasthenic crisis ..... *Bryan Young (London, ON)*
A case of rapidly progressive weakness with respiratory insufficiency .. *Charles Bolton (Rochester, USA)*
A patient with severe head trauma and possible brain death .... *Michael Diringer (St. Louis, USA), Bryan Young (London, ON)*

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A patient with primary cerebral haemorrhage
..... *Michael Diringer (St. Louis, USA)*
A comatose patient – cause is unclear
..... *Jeanne Teitelbaum (Montreal, QC)*

Medical Ethics in Neurology

Chair: Robert Nelson

Introduction: Why neurologists need ethics and why ethics need neurology ..... *Robert Nelson (Ottawa, ON)*
Neurological-ethical issues in end of life decisions ..... *James Bernat (Lebanon, USA)*
Ethical issues in neurology at the beginning of life ..... *Nuala Kenny (Halifax, NS)*
Ethical problems in genetic diseases ..... *TBA*
Ethics in neuroscience research *Henry Dinsdale (Kingston, ON)*

Challenges in Epilepsy for the New Millennium: Show Me the Evidence!

Chair: Alan Guberman

Cognitive and behavioural effects of AEDs ..... *Kim Meador (Augusta, USA)*
Tolerance to benzodiazepines and otherAEDs ..... *Alan Guberman (Ottawa, ON)*
Febrile convulsions ..... *Peter Camfield (Halifax, NS)*
The single seizure, an evidence-based medicine approach ..... *Sam Wiebe (London, ON)*
New AEDs and vagus nerve stimulation, are they worth the cost?..... *Richard McLachlan (London, ON)*
Epilepsy in the elderly ..... *Joe Bruni (Toronto, ON)*

Thursday June 15, 2000

Poster viewing/exhibits/breakfast

Meet the Expert Breakfast – Neurosurgery

Fernando Vinuela (Los Angeles, USA)

Plenary Session I: The Millennium and the Future of Clinical Neuroscience

Chairs: Gary Ferguson, Alan Goodridge

21st Century Neuroscience: Taking centre stage
Neurology: Richardson lecture .... *Richard Murphy (Montreal, QC)*
The future role of the clinician in the treatment of neurologic disorders in children ..... *Peter Camfield (Halifax, NS)*
Neurological and neurosurgical outcomes:Can they be measured and do they matter? ..... *Tom Feasby (Calgary, AB)*
Pathways for neural stem cell biology and brain repair ..... *Sam Weiss (Calgary, AB)*

Industry Course

Oral platform sessions

Poster viewing/exhibits/lunch

Plenary Session II: Endovascular Horizons in Cerebrovascular Disease

Chairs: Gary Ferguson, Alan Goodridge

Endovascular management of intracranial aneurysms: Present results and future technological developments
..... *Fernando Vinuela (Los Angeles, USA)*
Role of embolization in arteriovenous malformations of the pediatric and adult CNS ..... *Karel ter Brugge (Toronto, ON)*
From scalpel to catheter:The Zeitgeist in vascular neurosurgery ..... *Stephen Lownie (London, ON)*
Carotid angioplasty and stenting for carotid stenosis ..... *Robert Ferguson (Kingston, ON)*

Friday June 16, 2000

Poster viewing/exhibits/breakfast

Meet the Expert Breakfast – Neurology

Vladimir Hatchinski (London, ON)

Plenary Session III: Molecular Genetics and Clinical Neuroscience

Chairs: Gary Ferguson, Alan Goodridge

Unravelling the enigma of head injury
Neurosurgery: Penfield lecture ..... *Graham Teasdale (Glasgow, Scotland)*
From epilepsy genes to seizures: Identifying the gene is not enough
Canadian Society of Clinical Neurophysiologists Guest Lecture
..... *Philip Schwartzkroin (Seattle, USA)*
Gene therapy for nervous system diseases
..... *George Karpati (Montreal, QC)*
The molecular neuropathogenesis of HIV-induced neurological disease ..... *Chris Powers (Calgary, AB)*

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ORAL PLATFORM SESSIONS

POSTER VIEWING/EXHIBITS/LUNCH

NEUROLOGY DEBATE

Moderator: Alan Guberman
Resolved that we now have a rational basis forchoosing pharmacotherapy (both mono- and poly-) in epilepsy
Jack Schneiderman, (Toronto, ON), Kevin Farrell (Vancouver, BC)

NEUROSURGERY DEBATE

Moderator: Robert Broad
Acoustic Neuroma: Surgery or Radiosurgery or Both? .....
Michael Schwartz (Toronto, ON). Michel Bojanovski (Montreal, QC)

SATURDAY JUNE 17, 2000

CHILD NEUROLOGY DAY: PEDIATRIC NEUROBEHAVIORAL DISORDERS

Chair: Peter Humphreys

Neuroanatomy relevant to neurobehavioural disorders ..... *Peter Humphreys (Ottawa, ON)*
Tourette syndrome: The behavioural aspects .... *Roger Kurlan (Rochester, USA)*
The differential diagnosis of attention deficit disorder ..... *Wendy Roberts (Toronto, ON)*
PANDAS and its relationship to Tourette syndrome ..... *Roger Kurlan (Rochester, USA)*
Clinicopathologic conference ..... *Jean Michaud (Ottawa, ON)*
Autistic spectrum disorder from the neurology perspective .. *G. Robert De Long (Durham, USA)*
Autistic spectrum disorder, regressive type: The role of epilepsy ..... *Frederick Andermann (Montreal, QC)*
Psychopharmacologic agents in the management of pediatric neurobehavioural disorders .... *Normand Carrey (Halifax, NS)*

EMERGENT THERAPIES IN ACUTE STROKE

Chair: Stephen Phillips

Burning questions in experimental cerebral ischemia ..... *Antoine Hakim (Ottawa, ON)*
Magnetic resonance imaging in acute ischemic stroke ..... *Steven Warach (Bethesda, USA)*
Which antiplatelet agent regimen? . *Philip Teal (Vancouver, BC)*
What neurologists need to know about hyperlipidemia ..... *David Spence (London, ON)*
Thrombolysis I: Systematic review of the randomized trials ..... *Gordon Gubitz (Halifax, NS)*
Thrombolysis II: A year of CASES ..... *Alastair Buchan (Calgary, AB)*
Thrombolysis III: Practical tips for clinical decision-making ..... *Alastair Buchan (Calgary, AB)*
Stroke medicine in the new millennium ..... *Panel*

MULTIPLE SCLEROSIS

Chair: Mark Freedman

MS natural history studies of the last millennium are key to future drug evaluation ..... *George Rice (London, ON)*
MR imaging of MS: What the future holds ..... *Douglas Arnold (Montreal, QC)*
Diagnostic and treatment issues in MS: An interactive discussion ..... *Paul O'Connor (Toronto ON)*
New approaches to the management of bladder dysfunction ..... *Luanne Metz (Calgary, AB)*
Approaches to the treatment of secondary progressive MS ..... *Marika Hohol (Toronto, ON)*

MIGRAINE 2000: A NEW ERA IN MIGRAINE THERAPY?

Chairs: Werner Becker, Robert Nelson

Migraine treatment in the last century: Where have we come from? ...*Werner Becker (Calgary, AB)*
Migraine genetics: What do we know and what does it promise for the future? ..... *Dennis Bulman (Ottawa, ON)*
Spreading depression: What are its mechanisms and what are the potential therapeutic implications? ..... *Brian MacVicar (Calgary, AB)*
Brain serotonin receptors and the potential for better therapies in the future ..... *Edith Hamel (Montreal, QC)*
Symptomatic drug treatment: Where are we and where are we going? ..... *Allan Purdy (Halifax, NS)*
Prophylactic drug treatment: Current status, and can progress be expected? .... *Gordon Robinson (Vancouver, BC)*
Panel Discussion .... *Marek Gawel (Toronto, ON), Dennis Bulman (Ottawa, ON), Brian Mac Vicar (Calgary, AB), Edith Hamel (Montreal, QC), Allan Purdy (Halifax, NS), Gordon Robinson (Vancouver,BC)*

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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 PRESENTATIONS

Thursday June 15, 2000

Friday June 16, 2000

POSTER PRESENTATIONS

Thursday June 15, 2000 and Friday June 16, 2000

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2000 PRIZE PAPERS

HERBERT JASPER PRIZE

Mechanisms of Axonal Dysfunction after Chronic Spinal Cord Injury: Role of Altered Axonal Morphology, Myelination and Potassium Channel Expression

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

Background: Dysfunction of surviving axons which traverse the site of spinal cord injury (SCI) appears to contribute to neurological deficits. Although demyelination of injured axons and altered sensitivity to the K^+ channel blocker 4-aminopyridine (4-AP) have been implicated in mediating axonal conduction deficits, the underlying mechanisms remain unclear.

Methods: In this study, sucrose gap electrophysiology in dorsal column strips, histology, immunoblotting, and confocal immunofluorescence microscopy were used to characterize axonal physiology, changes in axonal morphology and to identify the K^+ channels that may be involved in axonal dysfunction after chronic (6-8 weeks postinjury) clip compression SCI of the thoracic cord at T7 in rats.

Results: Following chronic SCI, the injured dorsal columns displayed a reduced compound action potential (CAP) amplitude and conduction velocity, an increased threshold of activation, an increased refractory period, and displayed high frequency conduction failure as compared to the noninjured dorsal columns. The dorsal column had a significant number of injured axons with reduced myelin sheath thickness, but an overall increase in axonal diameter with examples of large axonal swellings. The K^+ channel blockers 4-AP and α-dendrotoxin (α-DTX), which block "fast" (rapidly activating) K^+ channels, resulted in a significant relative increase in the CAPamplitude of chronically injured dorsal column axons in comparison to control noninjured preparations. Western blotting and quantitative immunofluorescence microscopy showed an upregulation of Kv1.1 and Kv1.2 K^+ channel proteins on spinal cord axons following injury. In addition, Kv1.1 and Kv1.2 showed a dispersed staining pattern along injured axons in contrast to a paired juxtaparanodal localization in uninjured spinal cord axons.

Conclusions: In conclusion, these findings suggest that axonal dysfunction after SCI is contributed by an increase in axonal K^+ channel conductance, abnormally thin myelination, axonal swellings, in addition to other factors.

(Supported by MRC Canada, Easter Seal Research Institute, Ontario Neurotrauma Foundation/Rick Hansen Institute).

K.G. MCKENZIE PRIZE IN BASIC NEUROSCIENCE RESEARCH

Melatonin Enhances Acoustic Startle in the Rat and Human by Increasing Endogenous Opiates in the Amygdala

R.E. Mantle (Ottawa, Ontario), D.F. Cechetto (London, Ontario)

Background: Melatonin is the primary hormone produced by the pineal organ of the brain and is involved in multiple aspects of animal physiology related to circadian, seasonal and developmental timing, including cardiovascular control.

Methods: The acoustic startle reflex (ASR) pathway was electrically stimulated in anaesthetized male Wistar rats using an electrode placed stereotaxically in the medial geniculate ganglion. Various agents were injected by micropipette into the central nucleus of the amygdala (ACE) and the blood pressure response measured via an arterial line. Melatonin was delivered to the stomach by orogastric tube. In humans, 6 mg melatonin was given orally, and the blood pressure response to a standard acoustic noise stimulus was measured by finger cuff continuous sphygmomanometry after 30 min.

Results: In rats, melatonin given during the day enhances ASR to l69±72(SD)% (p=0.004, n=l3) of control, and to 188±94% (p=0.1, n=4) when blood melatonin is allowed to rise spontaneously at night. Oral melatonin also increased ASR to 177±95% (p=0.04, n=9) in human volunteers. In rats, dynorpin injected into the ACE increased ASR to 146±53% (p=0.02, n=6), while the general opioid antagonist naloxone decreased it to 53±38% (p=0.02, n=5) given in the same site. Naloxone in the ACE abolished the increased ASR caused by melatonin, and exposing rats to bright light abolished the spontaneous rise in ASR at night. Cobalt in the ACE had no significant effect on ASR.

Conclusions: 1) melatonin enhances acoustic startle in both rats and humans, 2) melatonin acts by increasing endogenous opioids in the amygdala, 3) tonic levels of opioids in the amygdala maintain acoustic startle, and 4) ACE modulates but does not contain synapses necessary to ASR. These results demonstrate a link between the pineal axis and neurocardiovascular control and provide further evidence linking endogenous brain opioids in cardiovascular hyperreactivity. These relations may play a role in the circadian clustering of adverse cardiac events in the early morning.

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The K.G. McKenzie Prize in Clinical Neuroscience Research

Initiating and Blocking Locomotion in Spinal Cats by Localized Application of Noradrenergic Drugs in Lumbar Segments

J. Marcoux, S. Rossignol (Montréal, Québec)

Background: After an IV injection of clonidine (α2-noradrenergic agonist) spinal cats (thoracic 13) can walk with the hindlimbs. Given that studies of neonatal rats have suggested that the rostral lumbar segments (L1-L2) play a critical role in the genesis of locomotion, we investigated the possibility of inducing or inhibiting locomotion in adult mammalian animals by restricted injections of noradrenergic drugs and also studied the importance of the rostral segments by sections at L3-L4.

Methods: Treadmill locomotion was evaluated using videotape and electromyographic (EMG) recordings. Clonidine or yohimbine (α2-noradrenergic antagonist) were delivered by making local pools or spinal micro-injections.

Results: Clonidine applied in baths only over L3-L4 or only over L5-L7 can induce walking. The locomotion evoked from one bath may be blocked by yohimbine applied in the other bath. Locomotion induced by IV clonidine can be blocked by micro-injections of yohimbine in L3-L4 or by sections at L3 or L4.

Conclusions: The neuronal networks responsible for locomotion are distributed over several lumbar segments. These networks can be activated through stimulation of limited segments but the integrity of other segments is necessary to maintain spinal locomotion.

Project supported by Christopher Reeve Paralysis Foundation and the MRC.

The President's Prize

Sudden Unexplained Death in Children with Epilepsy

Elizabeth J. Donner, Charles R. Smith, O. Carter Snead III (Toronto, Ontario)

Background: Sudden unexplained death is a significant cause of mortality in people with epilepsy. Risk factors that have been identified, including male sex, poor compliance with medications and increased number of antiepileptic drugs taken, may not apply to the pediatric population. Therefore, risk factors for SUDEP in children need to be evaluated independently from those in the adult population.

Methods: Cases of sudden unexplained death in epilepsy (SUDEP) in children less than 18 years of age occurring over a 10 year period, in the province of Ontario, Canada, were identified. Records were reviewed from demographic and clinical features, and neuropathology findings.

Results: Twenty-seven cases of SUDEP in children were identified. Sixty-three percent were male. Age at death ranged from eight months to 15 years. Fourteen children had symptomatic epilepsy, (52%). Five had cryptogenic epilepsy (18%) and eight had idiopathic epilepsy (30%). Twelve children were treated with one antiepileptic medication (AED) (46%), 10 were on two AEDs (38%) and three were on three AEDs (12%). At the time of death, seven children had one serum AED concentration below the therapeutic range (35%) and 12 children had AED levels within the therapeutic range (60%).

Conclusions: This case series represents the largest series of sudden unexplained death in children with epilepsy. At least two previously described risk factors for SUDEPin adults, low serum AED levels at time of death and AED polytherapy do not appear to be significant in children.

André Barbeau Prize

Neuropathological Changes in Huntington's Disease Cerebral Cortex and Associated CAG Trinucleotide Repeats

Sarah Furtado, N. Barry Rewcastle, Lisa Graham, Peter Bridge, Oksana Suchowersky (Calgary, Alberta)

Huntington's Disease is a degenerative disease of the central nervous system characterized by choreathetosis, dementia and an autosomal dominant mode of inheritance. Recent research has elucidated the neuroanatomical and neurochemical changes in striatum. Genetic research has determined that the disease is caused by an unstable trinucleotide repeat expansion on chromosome 4.

Much less research attention has been given to the study of cortical degeneration in HD. The purpose of this study was to examine the relationship between neuronal loss in HD frontal postmortem cortex and relate these changes to trinucleotide repeats and our previously published striatal study.

We counted neurons in layers 3 and 5/6 in two areas of frontal cortex, and after age at death was taken into account, performed correlation coefficients between these computed neuronal counts and the associated repeats for each case. Three of the four correlation coefficients were significant.

This study has shown a significant relationship between the loss of neurons in HD frontal cortex and associated repeats. The study suggests that the greater the number of repeats, the greater the neuronal loss and faster rate of deterioration. However, in comparison to our previous striatal study, the correlation coefficients are smaller, suggesting a different or slower pathological process in cortex than striatum in HD.

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ORAL PLATFORM PRESENTATIONS

PLENARY SESSION II

A-01

Aneurysms of the Distal Anterior Cerebral Artery

D.A. Steven, S.P. Lownie, G.G. Ferguson, (London, Ontario)

Background: Aneurysms of the distal anterior cerebral artery (DACA) are uncommon, comprising between 2-7% of all intracranial aneurysms. Located deep in the interhemispheric fissure, these aneurysms pose diverse clinical and technical challenges to the neurosurgeon.

Methods: The archives of all anterior circulation aneurysms managed at our institution between 1970 and 1998 were reviewed. Of 1109 cases of anterior circulation aneurysms, 59 patients (5.3%) with DACA aneurysms were identified. The clinical and surgical features of these 59 patients are described.

Results: There were 43 women and 16 men in the series. The mean age was 47 years. The typical clinical presentation was that of a classic subarachnoid hemorrhage with confirmatory CT findings. The aneurysm was usually small and customarily arose at the origin of the callosomarginal artery. Multiple aneurysms were identified in 51% of cases, most commonly on the middle cerebral artery. Fifty eight patients were operated upon, the majority through a right frontal paramedian craniotomy and interhemispheric approach. Rare proximal A2 aneurysms were approached via a pterional craniotomy and multiple aneurysms were generally approached through a large fronto-temporal craniotomy extended to the midline. The overall morbidity and mortality was 29% and 10.2% respectively with an operative mortality of 8.6%.

Conclusions: While uncommon, DACA aneurysms have many unique features. The characteristics of the aneurysms in this series confirm the findings of a number of smaller, previously reported series. With the aid of the operating microscope, an acceptable operative morbidity and mortality can be achieved.

A-02

The Effect of Regionalization on Outcome from Severe Traumatic Brain Injury (TBI)

David Steinke (Edmonton, Alberta)

Background: To evaluate the impact of trauma regionalization on outcome of patients with severe TBI.

Methods: Patient information was obtained from a prospective Trauma Registry for a period of 3 years pre and post-regionalization. During the initial 3 years (1993-96) all neurosurgical trauma was divided between 2 centers. During the last 3 years (1996-99) neurosurgical trauma was referred to one center. Information from the Trauma Registry was checked by review of the patient's chart. Patients were included with a post-resuscitation GCS of 8 or less. Trauma codes and patients with bilateral fixed and dilated pupils on admission were excluded. Outcome was evaluated with the Glasgow Outcome Score.

Results: There were 254 patients in the first group and 293 in the second. The groups differed in that patients in the more recent group had higher mean Injury Severity Scores (ISS) and mean ages ($P<0.05$). Also the number of patients with a lower GCS (3, 4 or 5) was greater in the 1996-99 study group ($P<0.05$). Despite regionalization, the time to admit patients was not significantly different. Patient outcome was worse following regionalization ($P<0.05$). However, the results of multivariate analysis showed that after adjusting for poor prognostic variables (ISS, age and admission GCS), patient outcomes were not significantly different. Sixty-six patients during the first time period and 50 patients during the second required "STAT" craniotomy. The outcomes for these patients were not significantly different.

Conclusions: Regionalization of Neurosurgical services to either one or two major centers in Edmonton has not affected outcome of patients with severe TBI. The concerns with respect to time to intervention and the effect delay may have on patient outcome were not born out in this study. The costs of regionalization are currently being tabulated and will be discussed at the time of presentation.

PLENARY SESSION III

B-01

Advanced Molecular Cytogenetic Approaches to Studying Brain Tumours

J. Bayani, M. Zielenska, P. Marrano, K. Ng, M. Taylor, V. Jay, J. Rutka, J.A. Squire (Toronto, Ontario)

Background: The karyotypic changes seen in brain tumours are generally still poorly understood. Traditional cytogenetic techniques have revealed some chromosomal aberrations in the various brain tumour types, but due to poor growth, chromosome morphology and the presence of complex structural rearrangements, many tumour samples remain not studied. The advent of more sophisticated molecular cytogenetic techniques, namely Fluorescence in situ Hybridization (FISH)-based-Comparative Genomic Hybridization (CGH) and Spectral Karyotyping (SKY) have circumvented some of these issues and have revealed more information on the genomic changes that occur in brain tumours.

Methods: In this study of 27 medulloblastomas and 8 astrocytomas we have employed classical G-banding analysis with CGH and SKY to reveal both the regions of net genomic change or regions of chromosomal rearrangement.

Results: In cases where there was available material, classical cytogenetics, CGH and SKY were carried out on the tumour specimens. Of the medulloblastoma cases, our data confirms previous reports of consistent chromosomal gains of chromosomes 17q and 7, however we have also identified chromosomes 3, 5, 6, 10, 13, 14, 18 and 22 to be more commonly involved in both structural and numerical rearrangements. Of the

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astrocytomas, along with whole chromosomal gains and losses, a cryptic structural change at distal 10q was detected as well as a novel amplification from chromosome 15.

Conclusions: Classical cytogenetic analysis provided the basic framework for characterizing gross karyotypic changes. FISH has allowed for identification of some chromosomal regions, but were limited to known sequences or genes. CGH served to circumvent the problems of growing tumours and enabled the detection of net gain and loss of chromosomal regions. Finally, the use of SKY has permitted the re-use of classical cytogenetic specimens to refine the detection of structural aberrations that may otherwise been undetected.

NEUROPHYSIOLOGY

C-01

Mechanisms of Axonal Dysfunction after Chronic Spinal Cord Injury: Role of Altered Axonal Morphology, Myelination and Potassium Channel Expression

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

Winner of the Herbert Jasper Prize. See page 8.

C-02

Familial Hirayama Disease: Clinical, Neurophysiological and Genetic Findings

M. Weber, G. Gibson, A. Eisen (Vancouver, British Columbia), Peter Andersen (Umea, Sweden)

Background: Juvenile focal amyotrophy of the upper extremity (Hirayama Disease) is characterized by insidious onset of painless weakness and wasting in a C7-T1 myotomal distribution. It develops mostly in young males between 15 and 25 years, is usually unilateral, and stabilizes after several years of progression. Only a few familial cases affecting male siblings have been reported.

Methods and Results: Bilateral weakness and wasting in a 40 year old male and his 42 year old sister started in an asymmetric fashion in their late teens, and progressed for several years prior to stabilization. The clinical picture in both siblings was identical. The first dorsal interosseus muscle and thenar eminence were more affected than the hypothenar eminence. Otherwise muscle bulk, strength, reflexes and sensory examination were normal. Nerve conduction studies were normal. EMG showed signs of active denervation in the clinically wasted muscles and chronic changes in unaffected muscle groups including the lower limbs. MRI of the head and cervical spine were normal. Genetic testing for the SMN gene and superoxide dismutase (SOD1) mutations are in progress.

Conclusions: This is the first report of a brother and a sister with bilateral focal non progressive amyotrophy. Widespread chronic neurogenic changes suggest a generalized anterior horn cell disease rather than a true focal amyotrophy and raise the possibility of a SOD1 mutation. The clinical, neurophysiological and genetic findings and a review of the literature will be presented.

C-03

The Chronic Model of Atypical Absence Epilepsy Induced by AY 9944 (AY) is Reproducible in C3H Mice. Artifact Free EEG Video Recording System (AFEEGRS) Data

M.A. Cortez, R.I. Servanescu, O.C. Snead III (Toronto, Ontario)

Background: Chronic mice models are commonly genetic mutations. To date, there are no developmentally induced chronic absence mice models.

Methods: Neonatal C3H mice (N=18) treated with AY (trans-1,4-bis[2-cloro-benzylaminomethyl]cycloexane dihydrochloride) (7 mg/kg) or saline every 6 days from postnatal day (PD) 2 to PD50. Cortical monopolar electrode implants were linked to a head connector-FET-preamplifiers-battery-signal conditioning device (5000x gain, 1Hz-100Hz filters, Axon Instruments), A/D converter (MP100 Biopac) and video/PC-PC video computer boards for recording image data, at PD 55.

Results: AFEEGRS recordings showed AY induced recurrent bilaterally synchronous spike-and-wave discharges (SWD) at 4-5 Hz, associated with staring, vibrissal twitching and ability to move during absence seizures, AY (n=9) mean ± SEM= 191 ± 32.1 vs. 55 ± 19.4 sec./h in controls (n=9), SWD duration mean difference 135.67, t= 3.17, df= 13, two tailed P value 0.0074, Unpaired test). AY mean SWD length ± SEM= 6.73 ± 0.63 vs. 3.27 ± 0.77 in controls (SWD Length difference 3.46, t= 3.44, df= 13, two tailed P value 0.0044, Unpaired test).

Conclusions: The AY 9944 model appears to be reproducible in C3H adult mice. Chronic atypical absence epilepsy can be induced in epilepsy prone mice after cholesterol biosynthesis inhibition during development.

GENERAL NEUROSURGERY

D-01

A Career in Neurosurgery?

T. Myles (Calgary, Alberta), S. McAleer (Dundee, Scotland)

Background: Medical students in Canada must make career choices during their final year of medical school. Selection of students for a career in neurosurgery has been based on marks, reference letters and personal interviews. Studies have shown that marks alone are not accurate predictors of success in medical practice; reference letters and interviews may be more important. This study was an attempt to assess the importance of, and ability to teach a number of personal skills and attributes that may be important to successfully complete a neurosurgical training program.

Methods: A questionnaire was sent to 185 active members of the Canadian Neurosurgical Society, asking them to give a numerical rating of the importance of 22 personal skills and attributes, and ability to teach those skills and attributes.

Results: Sixty-six (36%) questionnaires were returned. Honesty, motivation, willingness to learn, ability to problem solve, and ability to handle stress were the five most important

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characteristics identified. Neurosurgeons thought they could teach problem solving, willingness to consult informed sources, critical thinking, manual dexterity, and communication skills, but honesty, motivation and willingness to learn were among the most difficult to teach.

Conclusions: Honesty, motivation, willingness to learn, ability to problem solve and handle stress are important for success in a neurosurgical career. Reference letters and personal interviews should be structured to assess these attributes. Personal attributes that are difficult to teach should be possessed by applicants before acceptance into a training program.

D-02

Routine Scalp Shave for Cranial Procedures is Not Necessary

M.West (Cleveland, Ohio)

Background: Shaving the scalp has been a standard component of preparation for craniotomy for decades, despite a dearth of information supporting its need.

Methods: To assess the incidence of infection in patients prepared for cranial procedures without a scalp shave, this study enrolled, prospectively, 430 patients. No patient had a scalp shave. Patients were prepared pre-operatively with a shampoo of 4% Hibiclens soap on the evening before surgery. At surgery, the hair was parted along the proposed incision line and the scalp and hair were then prepared as usual with Hibitane scrub and paint. Patients received a single dose of Ancef 1gm. (or Vancomycin if an allergy was known) at induction of anesthesia. Surgical procedures included: 1.) Craniotomy a.) for trauma – 39; b.) vascular lesions – 108; c.) tumors – 142; d.) brain abscess – 5; e,) miscellaneous – 21; 2.) Shunts – 58; 3.) Stereotactic biopsies – 21; and 4.) Craniofacial procedures – 36.

Results: 3 postoperative infections occurred; one shunt, two craniotomies for tumor (operating time 7 and 8 hours respectively). Infections rate = 3/430 (0.7%).

Conclusion: Excluding the step of shaving the scalp pre-operatively does not increase the risk of infection for cranial procedures.

D-03

Cerebral Salt Wasting Syndrome in the Neurosurgical ICU: Definition and Incidence

S.K. Singh, D. Berry, A. Sharman, M.L. Halperin, M.D. Cusimano (Toronto, Ontario)

Background: Cerebral Salt Wasting Syndrome (CSWS) is defined by the presence of an intracerebral lesion, natriuresis despite contracted extracellular volume, and hyponatremia. However, the incidence of CSWS among neurosurgical patients remains poorly defined, and its diagnostic criteria are obscure. This study seeks to clarify the diagnostic features and incidence of CSWS.

Methods: A total of 10 patients with subarachnoid hemorrhage (n=6), closed head trauma (n=2), brain abscess (n=1), and brain tumor (n=1) underwent sampling of serum electrolytes every twelve hours and urine electrolytes every six hours. Net fluid and sodium balances were calculated for each patient over three time periods: the time from admission to the development of hyponatremia, between days 3 and 5 after neurosurgical insult, and for a total of 7-10 days.

Results: From admission to the development of hyponatremia, sodium and fluid balances varied. From days 3 to 5 following neurosurgical insult, all 10 patients exhibited negative salt and fluid balances compatible with CSWS. Most patients developed or were developing eunatremia by the end of the observation period.

Conclusions: The diagnosis of CSWS may be accurately made only when net sodium and fluid balances are calculated. The utilization of point values of urine sodium concentration to designate salt wasting does not adequately reflect the patient's net sodium balance over a period of time. Salt wasting may occur with a wide spectrum of neurosurgical lesions.

D-04

Effects of STN Stimulation Frequency on Motor Functioning in Parkinson's Disease

Z.H.T. Kiss, D.A. Grimes, B.A. Schwartz, C.L. Barclay, B. Hu (Ottawa, Ontario)

Background: In an unusual incident, a Parkinson's patient with a subthalamic stimulator (STN-DBS) returned to clinic complaining that she was worse. Upon interrogating her programmable generator, it was discovered that a spontaneous change in stimulation frequency had occurred from the usual 130 to 5 Hz. Whereas the frequency-dependent effects of thalamic stimulation are well known, little has been written on the effects of frequency in STN-DBS and this case prompted such investigation. The aim was to determine the effects of varying frequency of STN-DBS on parkinsonian features.

Methods: Two patients (4 sides) with Parkinson's disease were tested after being OFF drugs and OFF stimulation overnight. Movement time (MT), reaction time (RT), thumb-index rapid alternating movements (RAM), tremor frequency and acceleration were quantified repeatedly using a movement monitor (MM-1, Axon Instruments). The frequency of STN-DBS was altered from 0 to 185 Hz, at 30 minute intervals, maintaining the voltage constant. Five minutes of testing were alternated with 25 minute rest periods.

Results: We could not induce tremor with low-frequency (<20 Hz) STN stimulation. RAM improved with higher frequencies of stimulation. Low-frequency stimulation slowed MT in 1 of 4 sides.

Conclusions: Although it is commonly believed that low-frequency stimulation in thalamus may induce tremor, we were unable to demonstrate a similar phenomenon in the STN. This suggests that the two nuclei play different roles in tremorgenesis.

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NEURO-ONCOLOGY

E-01

Interdisciplinary Approach to Tumors of the Skull Base. Outcome and Functional Analysis in 160 Patients

F. Gentili, P. Gullane, D. Brown, J. Irish (Toronto, Ontario)

With few large series of patients reported, obtaining meaningful statistical analysis of outcome and quality of survival in skull base surgery remains difficult. We report on a series of 152 patients with skull base neoplasms treated by an inter-disciplinary team between 1982-1999. Seventy percent of the lesions involved the anterior cranial base and paranasal sinuses necessitating a craniofacial resection. Of 18 patients with esthesioneuroblastoma, 80% are alive with no evidence of recurrence at an average follow-up of 7 years. Of 20 patients with meningiomas that extensively transgressed the skull base, all are alive and fully functional at an average follow-up of 8 years with 7 patients having no evidence of recurrence. Tumor control rates for chordomas and chondrosarcomas (30) have been 64% and 95% respectively at 5 years. The most common malignant lesion was squamous cell carcinoma (SCC) of the paranasal sinuses with involvement of the skull base. The 2 and 5 year survival was 71% and 65% respectively with 53% being disease-free at 4 years. Although the overall post-operative complication rate was 40%, only 16% were considered serious. Functional status of the patients based on quality of life measures revealed 80% to be fully functional with less than 5% severely compromised. In conclusion, we believe an inter-disciplinary team approach utilizing modern skull base techniques has had a significant positive impact on functional survival in patients with neoplasms involving the skull base.

E-02

Intracranial Supratentorial Dermoid Cysts: A Review of 13 Cases

J.A. Shehadi, J.P. Farmer, J.L. Montes, K.M. Johnston, I. Alorany, D. Melanson, G. Bertrand, (Montreal, Quebec)

Background: Dermoid cysts are one of the most rare benign intracranial mass lesions with reported frequency between 0.04 to 0.06 % of all intracranial tumors. They most commonly occur along the midline and infratentorially. Supratentorial dermoid cysts are a rare subset of cranial dermoid cysts. In one series, only 8 patients with supratentorial dermoid cysts were seen in 37 years. In another series, only 7 patients were treated over a period of 21 years.

Methods: A retrospective review was made of all patients with histologically proven cranial dermoid cysts treated at the Montreal Neurological Institute, Montreal General Hospital and the Montreal Children's Hospital between 1970 and 1998. Patients with dermoid cysts limited to the skull bone or extradural space were excluded. Clinicopathological, radiological and surgical aspects of these cases were reviewed.

Results: There were 13 patients with histologically proven supratentorial intracranial dermoid cysts. Eight patients (62%) had lesions that were purely midline and 5 patients (38%) had lesions that were primarily or exclusively off the midline. Compared to patients with off midline dermoid cysts, patients with purely midline dermoid cysts presented at an earlier age, had a higher incidence of cutaneous manifestations and associated congenital abnormalities, but more often had a normal neurological examination. Patients with off midline lesions commonly presented with seizures and more frequently had a neurological deficit. Seventy-seven percent of these patients underwent complete surgical resection with good outcomes and no recurrences. Patients were followed for an average 5.7 years (ranging from 1 month to 13 years).

Conclusion: Supratentorial intracranial dermoid cysts are very rare benign lesions, which can frequently involve off-midline structures. Patients with purely midline lesions have a distinctly different clinical presentation from patients with lesions involving off midline structures. Surgical management of these lesions can yield good long-term prognosis.

E-03

Cell Differentiation Increases Invasion Rates in Primary Astrocyte Cultures.

J.X. Wilson, W. McDonald and R.F. Del Maestro (London, Ontario)

Background: Brain injury typically is followed by the differentiation of proliferative astroglial cells into reactive astrocytes. We hypothesized that increased invasiveness is a characteristic of the reactive astrocyte phenotype.

Methods: To evaluate this hypothesis, the invasiveness of neonatal rat astrocytes at different ages in culture (1-4 weeks) was studied in a 3-dimensional gel assay system (Vitrogen 100).

Results: The invasion rates of these astrocytes increased with age in culture until, after 3 weeks, it approached that of the C6 glioma cell line. Invasion was decreased by a metalloprotease inhibitor but not by scrine or cysteine protease inhibitors. Acceleration of cell differentiation of astrocytes by the protein kinase C modulator, PMA, increased the invasiveness of young cultures to the same levels as older cultures without altering collagen degrading activity.

Conclusions: Both spontaneous and PMA-induced differentiation increase astrocyte invasion rates. Metalloprotease activity is necessary for invasion but changes in collagenase activity may not contribute to the effects of differentiation on invasion rate.

E-04

Development of an Orthotopic Xenograft Meningioma Model

W.R. van Furth, M.D. Cusimano (Toronto, Ontario), I.E. McCutcheon (Houston, Texas), S. Laughlin, J.T. Rutka (Toronto, Ontario)

Background: Meningioma research has been hindered by lack of a valid and reliable *in vivo* model. The heterotopic location of the frequently used subcutaneous growing meningiomas, may seriously limit the clinical relevance.

Methods: Cells of the immortalized malignant meningioma

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cell-line Iomm-lee were injected intracranially in athymic mice.

Two injection techniques and two injection sites were used. In the convexity model, cells are implanted superficially, at the frontal convexity. In the skull-base model, cells are injected in a similar fashion, but directed at the skull-base. The cells are injected with a Hamilton syringe guided by a stereotactic device or a guide-screw. Tumor growth is evaluated by observation of symptoms and periodically MRI's.

Results: The convexity model consistently leads to tumor growth in the subdural and intraparenchymal locations. Tumor cell dissemination with CSF occurs and leads to an obstruction hydrocephalus. The skull base model tumors invade the bone and grow along the optic nerve. Stereotactically guided injection could be used in both models, while guide-screw guided injection resulted in unacceptable surgical mortality in the skull base model. T1 gadolinium enhanced MRI reliably shows end stage tumors.

Conclusions: This model may enable us to evaluate a variety of potential, non-surgical treatments for meningiomas.

E-05

Molecular Cloning, Genomic Structure and Mapping of Human *Suppressor of Fused (hSu(fu))*, a Candidate Tumour Suppressor Gene on Chromosome 10q24.3

M.D. Taylor, T.G. Mainprize, S. Scherer, J. Skaug, J.T. Rutka (Toronto, Ontario)

Background: The *Sonic Hedgehog (Shh)* signaling pathway has been shown to be overactive in human medulloblastomas (MB) due to mutations in upstream pathway members: *Shh*, *Patched* and *Smoothened*. Both humans (Gorlin's syndrome) and mice with germline mutations in the *Shh* receptor *Patched* develop MB. Although the majority of MB show evidence of increased *Shh* signaling, specific mutations have only been found in about 20% of tumours. The hedgehog signaling pathway has been well characterized in *Drosophila melanogaster*. We hypothesized that downstream inhibitors of *Shh* identified in *Drosophila* would be conserved in *H. sapiens* and might function as tumour suppressor genes.

Methods: Using the NCBI TblastN program we identified a human expressed sequence tag highly homologous to *Drosophila su(fu)*, a downstream inhibitor of hedgehog signaling. We designed nested primers for RACE (rapid amplification of cDNAends) on a human fetal brain library. RACE products were cloned into pT-Adv and sequenced. Clones were used to screen the Roswell Park Cancer Institute Bacterial Artificial Chromosome (BAC) Library. BACs were subcloned into pBluescript. Subclones were screened by PCR and sequenced to determine the genomic structure and exon/intron boundaries. RT-PCR of *hSu(fu)* was performed in 30 MB.

Results: We have identified a cDNA with extremely high homology to *Drosophila su(fu)* that we have named *hSu(fu)*. A genomic screen identified two BACs, 124G18 and 2F13 that contain genomic *hSu(fu)*. *hSu(fu)* has 12 exons and is highly GC rich in sequence. *hSu(fu)* maps to chromosome 10q24.3, a locus that frequently shows loss of heterozygosity in MB and glioblastoma multiforme. *hSu(fu)* is expressed in MB and normal brain consistent with a role as a possible tumour suppressor gene.

Conclusions: We have cloned a novel human cDNA for a gene in the *Shh* pathway and determined its' genomic structure. As *hSu(fu)* functions in a pathway important to medulloblastoma oncogenesis, maps to a locus frequently lost in medulloblastomas, and is expressed in medulloblastoma, it is an excellent candidate tumour suppressor gene.

E-06

Expression of Multidrug Resistance P-Glycoprotein in Human Brain Tumors

D. Shedid, M. Demeule, E. Beaulieu, R. Moumdjian, P. Ghosn, R. Beliveau (Montreal, Quebec), R. Del Maestro (London, Ontario)

Background: Multidrug resistance (MDR1) is associated with the expression of P-glycoprotein (P-gp), an ATP-dependent transporter which excludes anticancer drugs out of the cells. P-gp is highly expressed in the blood luminal membrane of the brain capillary endothelial cells that make up the blood-brain barrier.

Methods: P-gp was immunodetected by Western blot analysis in 50 human brain tumors including high grade gliomas (anaplastic astrocytomas, anaplastic oligodendrogliomas and glioblastomas), low grade gliomas (astrocytomas, pilocytic astrocytomas), meningiomas and schwannomas. Levels of P-gp were also determined in melanoma and lung adenocarcinoma brain metastasis as well as in 5 primary lung adenocarcinoma.

Results: P-gp levels were 10-folds higher in 70% of the meningiomas compared to the normal brain. Most samples of the other primary brain tumors expressed P-gp at the same level as the normal brain, except schwannomas in which it was reduced by 65%. P-gp levels were 70 and 95% lower in melanoma and lung adenocarcinoma metastasis, respectively, compared to the controls.

Conclusions: Most of the primary brain tumors (except schwannomas) retain their phenotype regarding P-gp expression. In addition, the high levels of P-gp in 70% of the meningiomas indicate that MDR, could be a marker for these brain tumors.

E-07

Transgenic Mouse Model of Malignant Astrocytoma: Astrocyte Specific Expression of Activated Ras

H. Ding, L. Roncari, P. Shannon, S. MacMaster, X. Wu, N. Lau, A. Nagy, A. Guha (Toronto, Ontario), D. Gutmann, (St. Louis, Missouri)

Background: 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.

Methods/Results: We have developed a transgenic mouse model of malignant astrocytomas, using the astrocyte-specific glial fibrillary acidic protein (GFAP) promoter to overexpress oncogenic Ras. In order to overcome the integration site dependent expression variations and high copy number integration related instability, we chose ES mediated

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transgenesis in which the transfected clones representing single transgenic integration site could be tested *in vitro* for astrocyte specific expression using retinoic acid differentiation. GFAP-RasV12 transgenic mice developed GFAP-positive multifocal astrocytomas postnatally. These tumors had a high mitotic index, nuclear pleomorphism, increased vascularity and VEGF expression, pathologically similar to human GBMs. Astrocytic cell lines isolated from these tumor mice demonstrated tumorgenic *in vitro* and *in vivo* growth when inoculated in syngeneic or immuno-compromised mice and inhibition of cell proliferation by farnesyl transferase inhibitor (FTI). Cytogenetic analysis of these tumor cells revealed amplification of several chromosomal regions which are syntenic with comparable abnormalities detected in human astrocytomas. These transgenic astrocytoma cells also have aberrant or loss of expression of relevant cell cycle regulatory proteins implicated in human astrocytomas, such as p16, p19, p53, PTEN, Rb, EGFR and CDK4.

Conclusions: Our transgenic mouse model shows many molecular and pathological similarities with human GBMs. This model may be useful to increase our understanding and pre-clinical evaluation of novel therapies in human GBMs.

NEUROSCIENCE

F-01

Immunofluorescent Confocal Analysis of HIV-1 Glycoprotein Neurotoxicity on Primary Human CNS Cultures

S. Iskander, R. Hammond (London, Ontario)

AIDS dementia complex (ADC) is the most common CNS degeneration in human immunodeficiency virus (HIV)-infected persons and results in a progressive dysfunction of cognitive and motor functions. Although the exact mechanism is unclear, evidence suggests the HIV transmembrane glycoprotein 120 (gp120) molecule plays a major role in HIV-associated neurotoxicity. Confocal microscopy for synaptic and dendritic markers on autopsy brain sections revealed that decreases in microtubule-associated protein 2 (MAP2) and synaptophysin immunoreactivity correlate with ante-mortem HIV-associated dementia. This suggested that neuronal dropout was not as strong a correlate for AIDS-related neuropsychiatric abnormalities as more subtle changes in the synaptic architecture of AIDS brains. We have developed and characterized a primary human culture system for long term maintenance of human CNS tissue. This *in vitro* system is capable of demonstrating the sub-cytocidal effects of gp120 exposure on the CNS, in the absence of lethal injury. Immunofluorescent analysis of our cultures reveal that gp120 exposed neurons share the same pathological features of sub-lethal dendritic damage found in post-mortem AIDS brains. This is the first time that the *in vivo* pathological correlates of AIDS dementia have been demonstrated *in vitro*, providing a sensitive model for the study of AIDS pathogenesis within the human CNS.

F-02

Unprecedented Blockade of Ischemic Spreading Depression by Dextromethorphan in Live Neocortical Slices

T.R. Anderson, A.J. Biedermann, C.R. Jarvis, R.D. Andrew (Kingston, Ontario)

Background: Spreading depression (SD) is a profound depolarization of neurons and glia that propagates like a wave across grey matter. During the first three hours of stroke, recurrent 'ischemic' SD increases neuronal damage and stubbornly resists pharmacological blockade. In contrast, SD without metabolic compromise (i.e. 'normotoxic' SD, as occurs in migraine aura) does not injure brain tissue and can be blocked by NMDA receptor antagonists. Brain cell swelling at the SD front and acute post-SD damage can be monitored in real time in live brain slices by imaging associated intrinsic optical signals (IOSs).[1]

Methods: The rat brain was excised under cold artificial cerebrospinal fluid (aCSF). A coronal slice (400 μm) of neocortex was superfused with aCSF gassed with 95% O_2 / 5% CO_2 at 37°C. For oxygen/glucose deprivation (OGD) experiments, N_2 replaced O_2 and [glucose] was lowered from 11 to 1 mM. Alternately, SD was induced by 100 μM ouabain, a Na^+/K^+ ATPase inhibitor. For recording the evoked field potential or the spontaneous negative shift (denoting SD), an extracellular micropipette was placed in layers II/III. IOSs were monitored as previously described.[1,2]

Results: IOS imaging clearly demarcated SD ignition and migration across the neocortical gray. If SD was induced by elevating $[K^+]_o$, the tissue fully recovered. However, in slices that were metabolically compromised by OGD or by ouabain exposure, acute neuronal damage developed where SD had propagated. Specifically, the evoked field potential was permanently lost and the cortical layers increased in opacity, indicating dendritic beading.[2,3] Glutamate receptor antagonists (100 μM kynurenate, 50 μM AP-5 or 10 μM CNQX) had no protective effect (n=25 slices), blocking neither SD nor post-SD damage. In contrast, 100 μM of the antitussive dextromethorphan blocked the onset of ischemic SD induced by OGD (n=9) or ouabain (n=11) and sustained the evoked field potential during 30 min of metabolic stress (n=3). Dextromethorphan also blocked normoxic SD onset (n=13) as did NMDAreceptor antagonists (n=8).

Conclusions: SD under ischemic conditions increases the metabolic load, thereby greatly exacerbating acute neuronal damage. The unprecedented inhibition of SD by dextromethorphan (probably mediated by sigma receptors) does not appear to involve glutamate receptors. We propose that neuroprotection *in vivo* imparted by this drug (when given immediately following stroke but not several hours later[4]) is the direct result of SD suppression.

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F-03

The Molecular Cascade in Human Temporal Lobe Epilepsy: Evidence for the Implication of Cyclooxygenase-2

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Background: Glutamate has been suggested to play a role in the pathogenesis of temporal lobe epilepsy. The stimulation of the glutamate receptors (NMDA) is associated with activation of calcium-dependent enzymes such as phospholipase A2, leading to accumulation of arachidonic acid and to its subsequent conversion into prostaglandins by cyclooxygenases. This molecular cascade can lead to severe neuronal cell death in CA1, CA3 and dentate gyrus of hippocampus.

Methods: To investigate this possible implication of cyclooxygenase-2 (COX-2) in the molecular cascade leading to drug-resistant epilepsy, we studied the CA1 subfield of surgical hippocampal specimens from patients with mesial temporal lobe epilepsy with (n=5) and without (n=2) hippocampal sclerosis, as well as from hippocampi of non-epileptic patients (n=2). Immunohistochemistry and reverse-transcription polymerase chain reaction (RT-PCR) were used to evaluate COX-2 expression. COX-2 expression was compared to expression of GFAP, synaptophysin and -actin.

Results: A significant increase of immunolabelling and mRNA of COX-2 was observed in sclerotic hippocampi of epileptic patients compared to non-epileptic patients, associated with an up-regulation of GFAP and decreased synaptophysin. Tissue from epileptic patients without hippocampal sclerosis present a COX-2 mRNA expression between that of sclerotic tissue and controls.

Conclusions: These results thus suggested that COX-2 likely plays a key role in the molecular cascade leading to drug-resistant temporal lobe epilepsy.

F-04

Intravenous Administration of a Novel Caspase Inhibitor Affords Neuroprotection Following Focal Ischemia in Rats

H. Li (Calgary, Alberta), N. van Bruggen (San Francisco, California), S.X. Cai (San Diego, California), AM. Buchan (Calgary, Alberta)

Introduction: The activation of caspases leads to post-ischemic neuronal death either through apoptosis or by inducing inflammatory responses in ischemic brain tissue. Caspase inhibitors injected intracerebroventricularly (ICV) reduce cortical infarction following focal cerebral ischemia. We tested the efficacy of a novel caspase inhibitor which could be administered intravenously (IV).

Material and Method: Male spontaneously hypertensive rats (SHR) were subjected to 90 minutes normothermic transient ischemia via middle cerebral artery occlusion (MCAO), followed by 22.5 hour survival. The Cytovia compound, CV1013, dissolved in 0.05 μM buffered TrisBase solution, was infused by IVbolus (20mg/kg) 60 minutes following the onset of ischemia followed by 6 hours of continuous infusion (5mg/kg/h). Physiological variables such as blood pressure, Po_2, Pco_2, pH, glucose and hematocrit were measured during ischemia. Neocortical infarction was measured using an imaging analysis system and percentage of cortical infarction over non-ischemic hemisphere was calculated.

Result: The animals treated with TrisBase as control sustained an infarct of 24 ± 7% (n=7) of hemispheric volume while for rats treated with CV1013, infarct volumes were reduced to 13 ± 6% (n=7) ($p < 0.01$). There were no temperature or physiological differences between groups to account for this difference.

Conclusions: This data demonstrates for the first time the efficacy of a systemically administered caspase inhibitor.

F-05

Diminished Injury-Related Nerve Hyperemia Following Peripheral Nerve Transection in Experimental Diabetes Mellitus

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

Background: Peripheral nerve regeneration is impaired in diabetes mellitus. Hyperemia following nerve injury may protect the nerve from immediate ischemia, by increasing local perfusion to the region. This study examined local nerve blood flow in a nerve injury model of experimental diabetes mellitus.

Methods: Diabetes was induced in Sprague-Dawley rats by streptozotocin (in citrate buffer). Left sciatic nerves underwent nerve conduction at 4 and 8 months of diabetes duration and then were transected. Laser doppler flowmetry (LDF) and hydrogen clearance polarography (HC) assessed nerve blood flow, particularly the hyperemic reaction, at 2 & 14 days following transection injury.

Results: Noninjured diabetic sciatic nerves exhibited slowed conduction velocity at both 4 & 8 month timepoints. There was no difference in baseline RBC flux measured by LDF between diabetic and control animals. Following transection, there were expected rises in local blood flow (2 & 14 days) in proximal and distal stumps of control nerves. In contrast, diabetic nerve stumps failed to show this rise in RBC flux.

Conclusions: Diabetic peripheral nerves lack a hyperemic rise in nerve blood flow following nerve injury. A deficient nutritive perfusion in diabetics may create an ischemic environment that is unfavorable to nerve regeneration.

Supported by MRC, AHFMR

F-06

Near Nerve Low Dose Opioid Analgesia in a Model of Neuropathic Pain

Wayne Truong (Edmonton, Alberta), Douglas Zochodne (Calgary, Alberta)

Background*:* Neuropathic pain is challenging to treat and may be resistant to opioid analgesics. Our lab has provided evidence that opioids have local physiological actions on inflamed or injured peripheral nerves. In this work, we addressed whether local opioids influence behavioural indices of pain in the Bennett and Xie (1988) chronic constriction injury (CCI)

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model of neuropathic pain.

Methods: CCI was created in male Sprague-Dawley rats using four loosely applied 4-0 chromic gut sutures around the sciatic nerve. Hyperalgesia was measured using the latency difference (CCI-control) to paw withdrawal from a thermal stimulus (Hargreaves et al, 1988). Morphine or its saline carrier were injected in a double masked fashion at the proximal CCI site under brief halothane anaesthesia 15 minutes prior to testing.

Results: At both 48h and 14d following CCI creation, near nerve morphine provided dose-related analgesia as indicated by the reversal of measurements of thermal hyperalgesia. Saline injections provided no analgesia. Doses of morphine effective locally were not effective systemically.

Conclusions: Local opioids provide analgesia in experimental neuropathic pain. Local opioid administration may provide a therapeutic alternative in instances of painful focal nerve injury.
Supported by MRC, AHFMR.

F-07

Neurotransplantation of Ventral Mesencephalic Cells in the Subthalamic Nucleus Attenuates Behavioural Deficits in the Parkinson Rat Model

K. Mukhida, S. MacKean, K.A. Baker, D. Sadi, I. Mendez (Halifax, Nova Scotia)

Background: Current neural transplantation strategies for Parkinson's disease (PD) focus on ectopic grafting of fetal dopaminergic cells in the caudate and putamen nuclei. Although such grafts ameliorate dopamine agonist-induced rotational asymmetry, they do not completely restore complex sensorimotor behavioural deficits and abnormal neuronal activity in other basal ganglia nuclei, including the subthalamic nucleus (STN). The aim of this project was to determine if the STN is an important target for neural transplantation in PD by assessing whether intrasubthalamic nucleus grafts can restore rotational asymmetry in the Parkinson rat model.

Methods: Seventeen female Wistar rats made hemi-parkinsonian with 6-hydroxydopamine were randomly assigned to one of three groups: one group (n=7) was transplanted with 800 000 embryonic day 14 fetal ventral mesencephalic cells in the STN, a second group (n=5) was transplanted with 800 000 embryonic day 14 fetal spinal cord cells in the STN, and a group (n=5) received injection of Dulbecco's modified Eagle's medium in the STN. Amelioration of behavioural deficits was assessed using the amphetamine challenge test. The animals were sacrificed seven weeks post-transplantation and the grafts analyzed using tyrosine hydroxylase immunohistochemistry.

Results: Animals that received injections of media or fetal spinal cord cell suspensions did not demonstrate improvement of amphetamine-induced rotational behaviour. In contrast, rats with fetal ventral mesencephalic grafts demonstrated significant attenuation of rotational asymmetry by six weeks post-transplantation.

Conclusions: These results demonstrate for the first time that dopaminergic reinnervation of the STN attenuates rotational asymmetry in the Parkinson rat model and suggest that the STN may be an important target in transplantation strategies for PD.

GENERAL NEUROLOGY

G-01

Neuropathological Changes in Huntington's Disease Cerebral Cortex and Associated CAG Trinucleotide Repeats

Sarah Furtado, N. Barry Rewcastle, Lisa Graham, Peter Bridge, Oksana Suchowersky (Calgary, Alberta)

Winner of the Barbeau Prize. See page S9

G-02

Inherited Myoclonus-Dystonia: Results from a 25 cm Genome Scan

D.A. Grimes, D.E. Bulman, L. Racacho (Ottawa, Ontario), A.E. Lang, P. St. George-Hyslop (Toronto, Ontario)

Background*:* Inherited myoclonus dystonia (IMD) is a new term that is now being used to describe an autosomal dominant form of myoclonus. We have identified a large 5 generation family with IMD and a genome scan was initiated in an attempt to identify a novel causative gene. Since starting the project IMD has been linked to chromosome 11q23 and a possible mutation identified in exon 3 of the dopamine 2 receptor gene (DRD2) in one family. A second family was also recently linked to a 28 cM region of chromosome 7q21-31.

Methods: In our IMD kindred thirty-two individuals have been examined, videotaped and have had blood drawn for DNA extraction. Twelve affected individuals meet published criteria for the diagnosis for IMD. 170 simple tandem repeat polymorphisms (STRPs) at an average density of 25 cM and covering the 11q23 and 7q21-31 regions were used to genotype all family members. Two point linkage analysis was performed using MLINK from the LINKAGE program.

Results: We excluded by linkage analysis and by direct sequencing the 11q23 region and DRD2 mutation in our family but found tentative linkage to the 7q21-31 region. The 170 STRPs have excluded (lod score < -2) approximately 40 % of the rest of the genome.

Conclusions: Independently we have obtained tentative linkage to the 7q21-31 region in our large family and are currently fine mapping this region to confirm or refute this preliminary finding.

G-03

Management Variations for Hemifacial Spasm

A.M. Kaufmann (Calgary, Alberta), P. Krawetz, D. Hobson (Winnipeg Manitoba), R. Ranawaya, T. Lye (Calgary, Alberta)

Background: Botulinum toxin (Botox) injections are often the primary treatment offered to patients with hemifacial spasm (HFS). We reviewed the clinical course of such patients, including those who subsequently elected microvascular decompression (MVD).

Methods: Data was collected from clinical records and questionnaires mailed to patients with HFS seen at two specialized centres in different Canadian cities.

Results: The 105 patients had HFS since age 19-76 years (52.2±13.6). The onset was mild in 53 and isolated to the periorbital muscles in 74. Disease progression was common, such that after 2-28 years (9.57±5.18), only 15% had isolated periorbital spasms and disease remained mild in less than 10%.

The majority of patients were treated with serial Botox injections (94/105), initiated 4.0±5.0 years after onset and repeated every 4.6±2.3 months. Ultimately, 33 of 105 patients elected MVD surgery. These rates were significantly different between centres (52% versus 17%; $p<0.05$).

Conclusions: Botox injections are particularly effective for isolated periorbital HFS, although do not halt the typical disease progression. The utilization of MVD surgery varies significantly between centres. Differences in satisfaction with long-term Botox therapy between the centers may reflect results of therapy. Alternatively, surgery offered at specialized centers where MVD is highly effective in providing cure of HFS may influence patient perception of non-surgical therapy.

G-04

MRSI Demonstrates Lack of Improvement in Corticoneuronal Integrity with Gabapentin Therapy in ALS

S. Kalra, Z. Caramanos, A. Genge, D.L. Arnold (Montreal, Quebec), N.R. Cashman (Toronto, Ontario)

Background: Proton magnetic resonance spectroscopic imaging (MRSI) can detect neuronal loss or reversible metabolic dysfunction by demonstrating a low N-acetylaspartate (NAA) relative to creatine (Cr) signal. MRSI has revealed improvement in corticoneuronal integrity with riluzole, a drug with proven clinical efficacy. A phase III placebo-controlled trial of gabapentin in amyotrophic lateral sclerosis (ALS) found no clinical benefit.

Methods: Nine ALS patients had MRSI scans before and 28±9 days after starting gabapentin. Eleven untreated ALS patients had two scans separated by 21±7 days. The change in NAA/Cr between paired scans was determined for 5 cortical regions.

Results: There was no significant change in NAA/Cr between paired scans in any region comparing the treated to the untreated group (mean change in NAA/Cr, p value): precentral gyrus (0.02, 0.73), postcentral gyrus (0.04, 0.12), superior parietal lobule (-0.23, 0.09), supplementary motor area (-0.09, 0.37), premotor cortex (-0.09, 0.30). Age, sex, duration between scans, and baseline NAA/Cr in the different regions was not statistically different between the groups.

Conclusions: MRSI did not show any consistent improvement in corticoneuronal integrity in ALS patients treated with gabapentin. This is in agreement with clinical studies establishing its lack of disease-modifying efficacy.

G-05

Seizures: Visualization, Dynamics and Control

H. Khosravani, P.L. Carlen, J.L. Perez Velazquez (Toronto, Ontario)

Background: Recent advances in the application of nonlinear time series analysis to slice and EEG recordings have permitted the characterization and prediction of events such as seizures. These methods are robust in providing a 'macroscopic' insight into the underlying dynamics of neuronal population behaviour.

Methods: The *in vitro* seizure model used relies on spontaneously generated seizure-like events (SLE) by superfusing rat hippocampal slices with artificial cerebrospinal fluid containing 0.5 mM Mg^{2+}. Epileptiform activity, recorded from the CA1 and/or CA3 area of the hippocampus, was analyzed by plotting the intervals between peaks in the recording (inter-peak-interval, IPI) during interictal and ictal-like events. Other data visualization aids were also used to quantify the activity.

Result: Transition to the seizure state was characterized by increased correlation between the timing of sequential peak events, characterized by a dynamic regime known as intermittency. The seizure represents the transient stabilization of a high frequency periodic state. Perturbation of the system by electrical stimulation during the pre-ictal state can suppress the SLE by stabilizing a different, low frequency state.

Conclusions: These results show that it is feasible to arrest seizures by perturbing the dynamics of the population during the pre-ictal state.

G-06

Neurologic Paraneoplastic Syndromes of Lymphoma: Mimics of Multiple Sclerosis.

P. Smyth, C. Hao, E.S. Johnson, M. Javidan, K. Warren (Edmonton, Alberta)

Background: Lymphoma paraneoplastic syndromes are many. They may mimic multiple sclerosis. We describe three cases with rare paraneoplastic lymphoma syndromes whose first presentations could be confused with multiple sclerosis.

Methods: Clinical methods.

Results: Case 1 involved a 59-year-old man who experienced aggressive recurrent bilateral optic neuritis. After one year, an occult non-Hodgkin's lymphoma was discovered in his lungs. Radiation therapy terminated further optic neuritis relapses for two years. Case 2 was a 57-year-old man who developed a progressive myelopathy characteristic of multiple sclerosis. MRIs and CSF remained persistently normal. Seven years later, Hodgkin's lymphoma of the spleen was found. With chemotherapy, his neurologic status stabilized. Our third case involved a 28-year-old lady who had been treated and "cured" for Hodgkin's lymphoma one year previously. She presented with a CNS demyelinating disease; clinical and neuropathological features were atypical for multiple sclerosis.

Conclusion: The pathogenesis of paraneoplastic syndromes has been associated with inflammatory features and autoantibodies. Our three cases may be examples of

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autoantibodies directed against the optic nerves, the spinal cord and CNS myelin respectively. A search for specific autoantibodies in these cases is required. Lymphoma paraneoplastic symptoms may resemble multiple sclerosis. A review of the literature and an algorithm of approach to these types of patients will be presented.

G-07

Florence Nightingale's Illness

John W. Norris (Toronto, Ontario)

Shortly after the Crimean War ended in March 1857, Florence Nightingale returned in triumph to England to be lionized by the public. Poems were written about her, she was the confidante of the Prime Minister, Lord Palmerston, and took tea with Queen Victoria. Her advice was sought on major health policies, and she was asked to design a new hospital in London (St. Thomas). A substantial bequest, produced by public subscription, was founded to fund an official nursing organization in Britain.

However, by early 1857, the terrible realization had come to Nightingale that, far from saving the troops at her base hospital in Scutari (just outside Constantinople), the wretched conditions proved more lethal than the Crimean battlefields. Eighteen thousand men had died, of an army of 25,000 but only 2000-3000 from wounds. Filth, dysentery, cholera and typhus had claimed the rest. Wounded soldiers, unable to be transferred to Nightingale's hospital in Scutari, had a much greater chance of survival in rough field hospitals set up near the battle zone.

In May 1857, Nightingale arranged the extensive destruction of letters and documents pertaining to what she now saw was a medical disaster, due to poor sanitation and infectious diseases. Shortly afterwards, from 1857-1868, she suffered a serious debilitating illness characterized by extreme fatigue, depression and lack of energy. Later medical historians have made several diagnoses, such as brucellosis, but the clinical picture corresponds much more closely to chronic fatigue syndrome. She subsequently made a spectacular recovery and died aged 90 in 1910.

CHILD NEUROLOGY

H-01

Sudden Unexplained Death in Children with Epilepsy

Elizabeth J. Donner, Charles R. Smith, O. Carter Snead III (Toronto, Ontario)

Winner of the President's Prize. See page S9.

H-02

Prognosis of Seizures Occurring in the First Year of Life

Anita Datta, Elaine Wirrell (Saskatoon, Saskatchewan)

Purpose: To determine if predictors of neurodevelopmental outcome and course of epilepsy can be identified in infants aged 1-12 months presenting with their first afebrile seizure.

Methods: All infants aged 1-12 months, presenting to the Royal University Hospital with new-onset, afebrile seizures between January 1, 1994 and December 31, 1998 were identified. Demographic data, details of the seizures (type, frequency, duration, etiology, treatment), developmental status, neurological exam at presentation and follow-up and test results (EEG, neuroimaging, metabolic, hematological, chemistry) were collected by chart review, interview with parents and neurological exam.

Results: Of 41 eligible subjects, 29 (71%) were contacted for follow-up, 3 (7%) were deceased but follow-up data was obtained from chart review, 8 (20%) could not be contacted but follow-up data was available from chart review and 1 (2%) could not be contacted and had no follow-up data available. The 40 patients with available follow-up data comprised the study group. The mean duration of follow-up from onset of epilepsy was 29 months (SD 17, range 1-64). Predictors of developmental and neurological abnormalities at follow-up included developmental delay and abnormal neurological examination at presentation, infantile spasms, lack of response to anti-epileptic drugs (AEDs), use of valproate and an abnormal EEG or neuroimaging study. Predictors against seizure control and remission of epilepsy and for the development of problematic seizures at follow-up included the use of valproic acid and failure to respond to AEDs.

Conclusion: Neurodevelopmental outcome of children with new-onset afebrile seizures in the first 1-12 months of life can be accurately predicted at the time of diagnosis with the aid of EEG and neuroimaging results. The course of epilepsy is more difficult to predict, but failure to respond to the first AED is worrisome.

H-03

Are There Changes in Intelligence and Memory Functioning Following Surgery for the Treatment of Refractory Epilepsy in Childhood?

S. Kuehn, D. Keene, P. Richards, E. Ventureyra (Ottawa, Ontario)

Rationale: In the treatment of children with refractory epilepsy, cortical resections have proven to be an effective means of achieving seizure control. There is minimal risk of permanent neurological sequelae associated with this procedure. Changes in the cognitive functioning of children who have undergone this procedure have not been well described. This paper presents the results of pre- and post-operative cognitive assessments in this patient group.

Method: Pre- and 6 month post-operative neuropsychological assessments which included standardized measures of intelligence and memory functioning, were conducted on children undergoing cortical resection for the treatment of epilepsy. Medical variables included: age at onset of seizures; age at surgery; site of resection; and degree of seizure control 6 months post-operatively. Group means were compared using Student t test.

Results: 31 patients met criteria for entering this study. Age at onset of seizures was 7 ± 5 years. Age at time of surgery was 12 ± 4 years. The pre-operative means for the group as a whole were: Verbal I.Q. 92 ± 17; Performance I.Q. 93 ± 19; Verbal

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Memory Index: 85 ± 20; Visual Memory Index: 99 ± 16. Twenty patients had resections involving the left hemisphere. The mean Verbal Memory Index for these patients was significantly lower than their mean Visual Memory Index, both pre- and post-operatively. No significant differences were obtained between pre- and post-operative means on any of the cognitive measures.

Conclusions: In this series, cortical resection in the treatment of epilepsy in children did not result in a significant change in performance on measures of intelligence or memory functioning.

H-04

Do Cognitively Normal Children with Epilepsy have a Higher Rate of Injury than their Non-Epileptic Peers?

Roxanne Kirsch, Elaine Wirrell (Saskatoon, Saskatchewan)

Objectives: To determine if cognitively normal children with epilepsy have higher accidental injury rates than their age and sex-matched friends without epilepsy, and what factors may predict this.

Method: Patients 5-16 years old, with a developmental quotient >70, without major motor or sensory impairments, with a one year history of epilepsy and who either had a seizure or had been on anti-epileptic drugs (AEDs) within the past year were identified from the pediatric neurology database of the Royal University Hospital. Twenty-five of 31 cases and their best friend controls agreed to participate. Seizure-related factors including type, duration, frequency, timing, date of diagnosis, AED initiation and discontinuation, specific types and total AEDs used, were assessed by interview. Questionnaires about accidental injury including type, number, severity, and, if applicable, injuries resulting from seizures, as well as, general safety practices, activity restrictions, and presence of ADHD, were completed by cases and controls.

Results: No significant differences in injury numbers (specific types or total), nor severity were found. Seizure-related factors did not predict injury in cases. Safety practices were similar, and restrictions in cases were not excessive. ADHD children had a higher injury rate, both in cases and controls.

Conclusions: Cognitively normal children with epilepsy do not have a higher injury rate than their non-epileptic peers. If consciousness is impaired in seizures, extra supervision for swimming and bathing, and restricted climbing heights are suggested. All other safety restrictions for epileptic children should follow those appropriate to non-epileptic children to allow a normal lifestyle.

H-05

Neuronal Ceroid Lipofuscinosis in Newfoundland: The Contribution of Juvenile Onset Disease

F. Costello, D. Buckley, S. Moore, J.C. Jacob, E. Ives, M. Frecker, P. Parfrey (St. John's, Newfoundland)

Background: The neuronal ceroid lipofuscinoses (NCL) are neurodegenerative lysosomal storage disorders with autosomal recessive (AR) inheritance. The various subtypes of NCL are differentiated on the basis of clinical features, age of onset, and pathological findings. Seven cases of juvenile NCL were identified with a view to determine the extent of genetic and phenotypic heterogeneity within this patient population.

Methods: A retrospective chart review was performed on all cases of NCL ascertained from the Division of Neurology from 1950 – 1999. Additional charts listed under the International Classification of Diseases (ICD) codes 333.0-333.9 from the provincial pediatric hospital were also reviewed. Further case information was obtained from pathological records of biopsy and/or post mortem specimens.

Results: Forty-eight cases of NCLwere identified, with seven meeting the clinical and pathological criteria for the juvenile type. These patients demonstrated clinical heterogeneity with respect to rates and onset of neurological regression, evolution of seizures, and disease course. Three of the juvenile cases were siblings and mutation analysis identified the common genomic deletion on chromosome 16p12 within this family. The results of DNAanalysis from the other cases are pending.

Conclusion: Juvenile NCL may be identified on the basis of clinical and pathological grounds. The use of molecular genetic techniques in the investigation of NCLwill have future benefit in the diagnosis of this neurodegenerative disorder. The investigation of the NCL patient population in Newfoundland is ongoing and may result in the identification of new genetic loci.

H-06

The Value of the History and Examination in Children with Neurological Problems

J. Dooley, K. Gordon, E. Wood, P. Camfield, C. Camfield, J. MacSween, E. Smith, W. Stewart (Halifax, Nova Scotia)

Rationale: To study the value of the clinical history, neurological examination and investigations in the evaluation of children with neurological problems.

Methods: 87 consecutive outpatient referrals to the Division of Pediatric Neurology were studied. At the time of receiving a letter of referral the consulting physician predicted the results of the history, neurological examination and the final diagnosis. Without access to the previous predictions, the physician completed the same questionnaire after the history, examination and after any investigation results became available. The data were analyzed using Epi-Info v 6.0.

Results: The correct diagnosis was predicted at the time of referral for 56 (64%), after the clinical history for 77 (87.5%) and after the examination for 85 (98%). The patient's diagnosis or management were considered influenced by the history for 26 (30%), by the examination for 11 (12.6%) and by investigations for 6 (7%).

Neither the examination nor investigations ever influenced the final diagnosis or outcome for children with: 1) headaches, 2) Tourette syndrome, 3) attention deficit or learning difficulties or 4) developmental delay. The examination influenced the outcome for 2 of 10 children with epilepsy, 2 of 5 with CP, and 7 of 29 with "other" diagnoses. Tests were influential in 3 of the 10 with epilepsy and 3 of the 29 with other diagnoses. In comparison, the history was considered to have affected diagnosis or management for patients in each diagnostic category.

Conclusions: The results from this ongoing study indicate

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that both the physical examination and investigations add little additional information for many children who are referred for neurological consultation, especially those with headaches, Tourette syndrome, ADHD/LD or developmental delay. In contrast the clinical history was valuable in patients in each diagnostic category.

H-07

Upper Limb Motor Function in Young Adults with Spina Bifida

Maureen Dennis, Michael S. Salman, Ross Hetherington, Brenda J. Spiegler, Daune MacGregor, James M. Drake, Robin P. Humphreys, F. Gentili (Toronto, Ontario)

Background: Little is known about adult function in individuals with neurodevelopmental disorders. In this paper, we describe upper limb motor function in young adults with spina bifida myelomeningocele (SB) and typically-developing age peers.

Methods: Participants were 28 young adults with SB, each having a Verbal or Performance IQ score of at least 70 on the Wechsler scales, and 28 age and gender matched controls, young healthy adults of normal intelligence. Four upper limb motor function tasks (posture and rebound of outstretched arms; limb dysmetria/dystaxia or finger-nose-finger coordination; and rapidly alternating hand movements or diadochokinesis) were performed under four different visual and cognitive challenge conditions: eyes open without counting; eyes closed without counting; eyes open and counting backward from 50; eyes closed and counting backward from 50. Motor independence was assessed by questionnaire.

Results: Fewer SB than control participants obtained perfect posture and rebound scores. The SB group performed less accurately than controls on limb dysmetria/dystaxia and diadochokinesis tasks, more slowly than controls on the diadochokinesis task, and they were more disrupted than controls by challenges during limb dysmetria/dystaxia and diadochokinesis tasks. Adaptive motor independence was unrelated to upper limb motor tasks, but higher rather than lower spinal lesions were associated with less motor independence.

Conclusions: Young adults with SB have significant limitations in upper limb motor function.

H-08

Canadian Paediatric Ischemic Stroke Registry: Analysis of Children with Sinovenous Thrombosis

Gabrielle deVeber and the Canadian Pediatric Ischemic Stroke Study Group: C. Adams, M. Adams, M. Andrew, F. Booth, B. Bjornson, D. Buckley, C. Camfield, A. Chan, S. Christie, R. Curtis, M. David, G. D'Anjou, G. deVeber, P. Flavin, G. Geoffroy, J. Gillett, P. Humphreys, D. Keene, S. Lanthier, S.E. Lee, E.A. MacDonald, D. MacGregor, S. Mayank, D. Meek, Pat. McCusker, B. Prieur, M. Shevell, B. Sinclair, J. Tibbles, E. Wood, J. Wu, J.Y. Yager.

Background: Childhood sinovenous thrombosis (SVT) is poorly understood. Understanding diagnosis, incidence, risk factors and outcomes enables rational treatment and design of therapeutic trials for this condition.

Methods: The Canadian Pediatric Ischemic Stroke Registry obtained standardized chart data on 160 neonates and children (aged less than 18 years) with radiographically proven SVT occurring from January 1992 to January 1998 at 16 pediatric tertiary centres.

Results: The incidence of SVT is at least 0.64 per 100,000 children / yr. (95% CI 0.55-0.78). Neonates comprise 38% of patients. Gender is equal except in neonates where males predominate (63%). Venous infarcts are present in one half and are hemorrhagic in two-thirds and bland in one-third. Clinical presentations are: increased intracranial pressure (72%), seizures (59%) and neurological deficits (56%). The diagnosis is missed by computerised tomography (CT) in 11% of patients. The predominant sinuses involved are: lateral sinus (50%) and superior sagittal sinus (42%). Risk factors, definable in 98% are frequently multiple and include: dehydration, (36%), prothrombotic disorders (26%), head and neck infections (19%), perinatal complications (17%), other hematological disease (16%), head and neck pathology (16%), connective tissue disease (13%), procoagulant drugs (10%), sepsis (8%) and others (29%). Over half of the patients receive anticoagulant therapy consisting of: low molecular weight heparin (59%), standard heparin (42%), coumadin (46%), aspirin (12%). Outcome consists of: normal (57%), neurological abnormality (36%) and death (7%). Seizures at follow-up occurred in 19%. Recurrent thromboses occurred in 12%, (12 cerebral, 5 systemic).

Conclusions: Paediatric SVT is not rare. CT alone is insufficient for diagnosis. Given current treatment practice and significant morbidity, recurrence and mortality, randomised trials are needed to define the role of anticoagulant therapy.

GENERAL NEUROSURGERY

I-01

Melatonin Enhances Acoustic Startle in the Rat and Human by Increasing Endogenous Opiates in the Amygdala

R.E. Mantle (Ottawa, Ontario), D.F. Cechetto (London, Ontario)

Winner of the K.G. McKenzie Prize in Basic Neuroscience Research. See page 8.

I-02

Initiating and Blocking Locomotion in Spinal Cats by Localized Application of Noradrenergic Drugs in Lumbar Segments

J. Marcoux, S. Rossignol (Montréal, Québec)

Winner of the K.G. McKenzie Prize in Clinical Neuroscience Research. See page 9.

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I-03

A Role of Percutaneous Radiofrequency Neurotomy of Posterior Primary Ramus in Management of Chronic Low Back Pain

J.Y. Park (Seoul,Korea), T.H.Cho (Seoul,Korea), H.K. Lee (Seoul,Korea), J.K. Suh (Seoul,Korea)

Background: Although the term "facet syndrome", first coined by Ghormley, has existed more than 60 years it still remains an undefined entity. But, presently there are no known pathognomonic, radiographic, historical, or physical examination findings that allow one to definitively identify lumbar facet joints as pure source of low back pain. The purpose of this study is to prospectively evaluate the role of facet denervation (radiofrequency neurotomy of medial branch of posterior primary ramus) in more strictly selected patients with low back pain based on two temporary diagnostic blocks (lidocaine and saline in double-blinded fashion).

Methods: A total of 63 patients who met all inclusion criteria and responded to temporary block were included. Main inclusion criteria were axial and predominantly proximal (above knee) pseudoradicular pain exacerbated by extension and facetal irritation by pressing down on the knee with leg positioned in figure of "4", but not associated with clinical signs of motor, sensory deficits, sciatic compression, and radiographic findings suggestive of prominent disc or lesions of roots and cord. Patients must have had more than 6 months of pain and failed to obtain substantial benefits from at least 4-6 weeks of intense physiotherapy. Eighteen patients who had previously undergone lumbar disc surgeries but had persistent low back pain who met above criteria were also included.

Results: There were 39 males and 24 females (median age 47.4 years) with a median duration of back pain 14.7 months (range, 6-33). The RF procedure was done under local anesthetics and performed according to side(s) of pain, but covered at least 3 levels of the dermatome. The minimal follow-up period was 24 months. Initial responders (>50% of pain relief at first follow up) were 74.6 % (47/63). At 6 months, they were reduced to 60.3%, but 52.3% of patients were still responders at 2-years follow up. Variables such as sex, age, and previous surgery showed no significant relationship to outcome. Variables found to be not significant but have a tendency to be related to outcome were clinical findings including positive sign of "4", bilaterality, older age. There were no major neurologic complications or deaths related to procedures, however 2 patients had dysesthesia for over 3 months.

Conclusions: These results indicate that percutaneous RF neurotomy of the posterior primary ramus may play a role in the management of patients with a specific clinical syndrome, presumably chronic low back pain of mechanical origin from facet joints or surrounding structures. It is considered safe and may be repeated, with similar success, even when pain recurs. Similar results obtained in patients with previous disc surgery may also have a role in management of selected patients with failed back surgery syndrome.

I-04

Injury Prevention in the Community: An Evaluation of the Think First for Kids Program

M.D. Cusimano, A. Sharman, R. Coulthard, M. Chipman, B. Freedman, C. Tator (Toronto, Ontario)

Background: Injuries to Canadian youth are the most unappreciated public health issue facing Canadians. The Think First for Kids Program (TFFK) aims to prevent injuries to Canadian youth by a multifaceted program with a school-based educational program at its core. The purpose of this study was to evaluate the effectiveness of the program given to children in grades 1, 2 and 3.

Methods: Tests assessing student knowledge (and behaviour) were given to 584 "active" students (25 classrooms) before and after the delivery of the TFFK program. Tests were also given to 596 "monitoring" students (27 classrooms) before and after a six-week interval where the program was not delivered. Questionnaires were administered to teachers and parents in both types of schools to assess the degree of program implementation. Total percent scores were analysed by means of the t-test statistic ($p<0.05$).

Results: Baseline scores were equivalent for both groups. Students in all 3 grades of the active schools showed significantly better improvements in knowledge than those in control schools. Test retest reliability of the measures used was good ($p < 0.01$).

Conclusions: The TFFK has been successful at improving children's knowledge of safe practices and behaviours. Future work aims at looking at the relationship between knowledge, behaviour and outcomes.

I-05

Outcome Analysis of Acute Traumatic Subdural Hematoma in the Elderly

F. Durity, R. Perrin (Vancouver, British Columbia)

Background: Recent focus on resource allocation in health care requires doctors to find cost effective treatments without adversely affecting patient outcome. The notoriously poor outcome of acute traumatic subdural hematoma (ATSDH) correlates closely with advancing age and low Glasgow Coma Score (GCS). We estimate the health care costs of this cohort, regardless of outcome.

Methods: A consecutive, unselected series of patients from January 1990 to December 1997 (N=21), age ≥70 years and with admission GCS scores of ≤8 were reviewed. Their clinical charts and computerized tomographic scans were reviewed. Neurological features (e.g. brain stem reflexes), and associated co-morbidities were noted. Their clinical outcome and health care costs in current dollars were tracked.

Results: 12 of the 21 patients were managed non-operatively; 11 died and 1 survived in a dependent state. 9 patients underwent craniotomy; 5 died and 4 survived but only 2 achieved modest independence. All survivors had prolonged costly health care (to be presented in detail).

Conclusions: We conclude that ATSDH in this patient group

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is usually lethal and that the occasional survival with craniotomy is costly with questionable quality of life. A larger cohort needs study to facilitate selection of "favourable outcome predictors" if any in this group.

I-06

Intra-operative Magnetic Resonance Imaging in Temporal Lobe Epilepsy

R. Heale, M.A. Lee, G. Sutherland, N. Pillay, R. Sevick, T. Myles (Calgary, Alberta)

Background: The extent of medial temporal lobe resection for the treatment of temporal lobe epilepsy correlates with outcome. It is difficult for surgeons to visually estimate the amount of medial tissue excised. Image-guided systems improve documentation of extent of tissue removal but may become inaccurate due to progressive brain shift. Intra-operative MR imaging provides accurate documentation of the extent of medial temporal or lesion excision prior to wound closure.

Methods: Between October and December, 1999, 6 patients with temporal lobe epilepsy had their surgical procedure monitored using intra-operative MRI. There were three males and three females, aged 17 to 42 years, whose epilepsy was refractory to medications. Two females and one male had mesial temporal sclerosis, one female had a vascular malformation, and one male had a ganglioglioma diagnosed on pre-operative MRI. One patient had a normal pre-operative MRI. All were scanned at the beginning of surgery and following excision of as much of the lesion or hippocampus as seemed necessary. A combination of axial and coronal T1 and T2 weighted images were used.

Results: In all patients there was residual lesion or hippocampal tissue detected on inter-dissectional MR imaging which was subsequently removed. Quality assurance imaging confirmed the completeness of each resection. Presently, five of six patients are seizure free following surgery.

Conclusion: Intra-operative MR imaging is the most accurate method presently available to determine extent of tissue removal during neurosurgery. It may lead to improved outcome for patients undergoing temporal lobe resections for epilepsy.

I-07

Neuroendoscopy: Experience with 110 Patients

M.G. Hamilton, S.T. Myles, J. Vecil, I. Fleetwood (Calgary, Alberta)

Neuroendoscopy is becoming an essential part of comprehensive neurosurgical adult and pediatric patient care. We have seen a steady increase in utilization since the introduction of neuroendoscopy five years ago at the University of Calgary. We have now treated 110 patients during 120 operative sessions, performing 150 separate neuroendoscopic procedures. This patient population consisted of 60 pediatric and 50 adult, 63 male and 47 female patients. The most common procedure performed was third ventriculostomy (n=44), with 11 patients undergoing removal of their (pre-existing) malfunctioning ventriculo-peritoneal shunt systems. Twenty-four tumor biopsies were performed, including four craniopharyngioma cyst decompressions. Eleven colloid cysts have been removed. The neuro-endoscope has also been utilized during four spinal cord detethering operations. Five patients have died, four secondary to progression of disease (brain tumor) and one from overwhelming nosocomial sepsis. The most common morbidity has been intraventricular bleeding (n=3) with no patient requiring external ventricular drainage or craniotomy for treatment. All morbidity will be reviewed. We have established a local database and are striving to establish a Canada-wide database to more fully document the efficacy and morbidity associated with neuroendoscopic procedures.

I-08

Microvascular Decompression Failures: Lessons Learned from Re-Explorations

A.M. Kaufmann, K. MacDougall (Calgary, Alberta)

Background: Results of microvascular decompression (MVD) surgery are highly dependent upon details of technique, and a study of surgical failures is instructive.

Methods: This report describes the surgical findings and outcomes from 21 re-explorations for persistent or recurrent trigeminal neuralgia (TN) and hemifacial spasm.

Results: The senior author performed 175 MVD procedures between June 1996 and December 1999. Twelve patients were referred after an unsuccessful MVD. At re-exploration there was significant arterial vessel compression upon the trigeminal (10) or facial (2) nerves, due to ineffective placement of various implant materials. The results of "redo-MVD" were excellent or good in 7/8 with typical TN, 2/2 with HFS and 0/2 with atypical TN.

In nine other patients with recurrent TN, shredded Teflon felt implants maintained the first decompression, although new vascular compression was due to AICA(2), veins (4), and small arteries (1). "Redo-MVD" results were excellent in 4/7. Two others had no new compression and partial rhizotomies were performed. There were no complications such as stroke, hemorrhage, infection, deafness or other cranial nerve palsies. One patient had a transient CSF leak treated with lumbar drain for 3 days.

Conclusions: Inadequate alleviation of vascular contacts is often seen in patients with failed MVD, while new nerve root compressions may also develop. Re-exploration is effective an treatment for many patients with recurrent of persistent trigeminal neuralgia and hemifacial spasm, when a thorough MVD is performed.

CEREBROVASCULAR DISEASE

J-01

Is Cervical Arterial Dissection Ever Spontaneous?

V. Beletsky, Z. Nadareishvili, J. Norris – for the Canadian Stroke Consortium (Toronto, Ontario)

Background: Dissection of the carotid or vertebro-basilar arterial system is a major cause of ischemic stroke in the young (<45 yrs). In certain cases the traumatic etiology is not in doubt,

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but sometimes arterial dissection appears to be entirely spontaneous. A critical factor in this decision-making is the time course of events.

Methods: The Canadian Stroke Consortium is presently conducting a prospective case-controlled study to examine the basic clinical features of pathogenesis of dissections.

Results: Of 56 cases 42 were proven traumatic (9 carotid and 33 vertebral) and 14 apparently spontaneous (10 carotid and 4 vertebral) dissections. "Violent" trauma (e.g. neck manipulation) caused 18 dissections, while 24 traumatic cases were related to non-violent trauma (golfing, heavy lifting, etc.). The mean time course in the traumatic group was 2.5 days. In the spontaneous group 3 patients had connective tissue disorders, and in 5 a possible preceding event was suspected.

Conclusions: Trauma is the major etiology in cervical arterial dissection. There is a spectrum both of trauma from severe to minor, and of genetic weakness in the vessel wall. Where the threshold of one ends and the threshold of the other begins must remain speculation until more data are available.

J-02

An Analysis of Patient Eligibility forAlteplase in Acute Ischemic Stroke

Philip A. Barber, Jinjin Zhang, Andrew M. Demchuk, Michael D. Hill, Andrea Cole Haskayne, Nancy Newcommon, Alastair M. Buchan (Calgary, Alberta)

Background: Alteplase has been suggested to be an effective therapy in acute ischemic stroke. However, its use in acute stroke will not have a major impact on death and dependency unless it is widely accessible, appropriate, safe, and effective in the vast majority of patients.

Methods: Data was collected from acute stroke patients from an admission registry between October 1996 and December 1999. Information collected included time of symptom onset, time of arrival at the emergency department, when first seen by a physician, reason for not using t-PA, and causes of delay between time of symptoms occurring and arrival at the hospital. The stroke type and syndrome classification were recorded based on clinical symptoms and signs and neuroimaging.

Results: Of the 2198 presenting to the emergency department 50.5% were diagnosed as ischaemic stroke, 28% intracranial hemorrhage (intracerebral, subarachnoid or subdural), and 12 % related to transient ischemic attack. Three hundred and forty nine patients were admitted within 3 hours of stroke symptom onset. Alteplase was administered to 86 acute ischemic stroke patients intravenously and 15 received intra-arterial therapy. The major reason for exclusion of those eligible in terms of time were rapid resolution of symptoms (26.2%), mild stroke (26.6%) and specific contraindications (10%). However, 11% of these patients would have potentially fulfilled NINDS criteria but were not treated. The major reason for delay in presenting was uncertain time of symptom onset (40%).

Conclusion: The success and cost effectiveness of thrombolytic therapy demands that more patients are made eligible for this treatment. This can be done by understanding why patients are excluded from this therapy and the cause of time delay.

J-03

tPA Use forAcute Ischemic Stroke in Southwestern Ontario: Safety and Efficacy Using CT Criteria

B. Silver, B. Demaerschalk, A. Tamayo, A. Devasenapathy, J. Merino, E. Wong, J.D. Spence, G.B. Young, C. O'Callaghan, V. Hachinski (London, Ontario)

Background: A 1995 NINDS study found benefit for the use of intravenous tissue plasminogen activator (tPA) in acute ischemic stroke (AIS). The symptomatic intracranial hemorrhage (SIH) rate in the study was 6% which has deterred some physicians from using this medication. tPA was given approval for the treatment of AIS in Canada in February 1999.

Methods: Patients in the London, Ontario region were treated according to NINDS study criteria with one major exception; those with > 1/3 involvement of the idealized middle cerebral artery territory on neuroimaging were excluded from treatment.

Results: 23 patients were treated [median pre-stroke Rankin 0, median post-stroke Rankin 5, median post-stroke NIH stroke scale score (NIHSS) 13]. No SIH was observed. 4 point or greater improvement in NIHSS was seen in 61% of patients at 24 hours. 41% were discharged directly home. Three month data are complete for 15 patients: 13% died, Rankin 0-1 in 40%, NIHSS 0-1 in 27%.

Conclusions: Compared to the NIH study, similar beneficial effects were seen without similar risk of SIH. These findings suggest that imaging exclusion criteria may lessen the risk of SIH without compromising positive benefits; the potential reduced risk may increase the use of this medication for stroke.

J-04

The Hyperdense Sylvian Fissure Branch Sign: An Early Marker of Thromboembolic Stroke

Philip A. Barber, Andrew M. Demchuk, Mark E. Hudon , Warick Pexman , Michael D. Hill, Jinijin Zhang, Alastair M. Buchan (Calgary, Alberta)

Background: The hyperdense appearance of the middle cerebral artery is now a familiar early warning of large cerebral infarction, brain oedema and poor prognosis. Less well described, however, is the hyperdensity associated with embolic occlusion of branches of the middle cerebral artery seen in the sylvian fissure. The aim of this study was to define, determine the incidence, diagnostic value, and the reliability of this sign.

Methods: Computed tomographic (CT) scans performed on patients with acute ischemic stroke within 3 hours of symptom onset were analysed for signs of thromboembolic stroke and evidence of early CT ischemia. Two pairs of neuroradiologists and stroke neurologists evaluated scans for the presence of the hyperdense sylvian fissure branch sign (HSFBAS), the hyperdense MCA sign (HMCAS) and for degree of MCA territory involvement.

Results: Of 100 consecutive patients presenting within 3 hours of symptom onset, 90 were considered at symptom onset to have anterior circulation stroke syndromes. All patients received intravenous tissue plasminogen activator. HMCASs were seen in 3% of CTscans whereas HSFBAsigns were seen in

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20%. The NIHSS associated with a HSFBAsign ranged from 5-31 (median 15). All CT scans which showed evidence of a HSFBA sign had infarction on the follow-up scan either involving the insula or frontalparietal cortex. Fifty percent of those with a HSFBA sign were dependent or dead at 3 months. The interobserver reliability between the clinicians for the detection of HSFBA sign was in the moderate to good range (Kappa 0.35-0.70).

Conclusions: The hyperdense sylvian fissure branch artery sign has a high incidence in a group of ischemic stroke patients presenting within 3 hours of symptom onset and suggests thrombotic or embolic occlusion of a MCA branch artery. The sign predates early CT ischemic change and may be helpful in its early detection.

J-05

Regional Access to Acute Stroke Intervention: the Southeastern Ontario Experience

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Background: Southeastern Ontario is a large geographic area covering more than 20,000 square kilometres. On July 26, 1999, all ambulance services began bypassing the closest hospital to go directly to Kingston General Hospital (KGH) with patients who meet the criteria for the "Acute Stroke Protocol". This protocol is a coordinated system response by dispatch, paramedics, physicians, community service providers, emergency and inpatient staff in community hospitals, and the KGH Acute Stroke Team. The goal is to ensure equitable access to diagnostics and new interventions for acute stroke such as recombinant tissue plasminogen activator (rt-PA), available only at KGH.

Methods: Protocol implementation involved region-wide planning and intensive training for over 500 dispatchers, paramedics, and nurses. Thirty-four organizations now triage and transport acute stroke patients using consistent criteria and terminology.

Results: As of January 11, 2000, 153 stroke patients were transported to regional hospitals, the acute stroke protocol was activated 83 times and 23 patients from communities across Southeastern Ontario received rt-PA.

Conclusions: Patients now have improved access to diagnostics and new interventions for stroke under the acute stroke protocol. A repatriation process and community-based care pathways are in development to ensure standards of care across the region.

J-06

The Canadian Activase for Stroke Effectiveness Study (CASES)

Michael D. Hill, Alastair M. Buchan for the CASES Investigators (Calgary, Alberta)

Background: Therapy for acute stroke using rtPA was approved in Canada in February 1999. The Canadian Activase for Stroke Effectiveness Study Group was formed to study the use of rtPA in Canada in a 2 year post-marketing study.

Purpose: To both prospectively assess the safety of rtPA in the Canadian context and to examine whether the efficacy of rtPA for acute stroke, demonstrated in the NINDS trial, can be translated into effectiveness in routine clinical practice across Canada.

Methods: The CASES group is a collaboration among the Canadian Stroke Consortium (CSC), the Heart and Stroke Foundation of Canada, Hoffman-LaRoche Canada and physicians across the country. Centres across the country were registered and recruitment is ongoing. Patient information is being collected prospectively and evaluated in a blinded fashion. The study protocol has been approved by the research ethics board at each centre. Demographics, stroke risk factors, blood pressure, biochemistry, hematology, and CT scans are being collected. NIHSS and mRS scores are being collected. Outcomes will be monitored at discharge and at 3 months.

Results: In the first five months, 57 centres are registered. 226 patients have been treated to date. The symptomatic hemorrhage rate is 4.4% (2.1% to 8.0%). 90-day outcomes are listed in the table.

90-day outcome measure (n=108)	
Median modified Rankin scale score	3
• Independent (mRS 0-2)	48%
• Dependent (mRS 3-5)	36%
• Dead	16%
Median NIHSS score	3
Living at home	81%

Conclusions: CASES is an ongoing prospective evaluation of the effectiveness of rtPA in acute stroke. The symptomatic hemorrhage rate is 4.4%. 90-day outcomes are commensurate with those observed in randomized trials.

J-07

Implementation of an Acute Stroke Protocol in an Academic Hospital: Successes and Lessons Learned

C. O'Callaghan, B. Silver, B. Demaerschalk, A. Tamayo, J.G. Merino, E. Wong, S. Deshpande, E.Denomy, D. Karcz, J.D. Spence, V. Hachinski, G.B. Young (London, Ontario), A. Devasenapathy (Hershey, Pennsylvania)

Background: Following approval of Tissue Plasminogen Activator (tPA) for stroke by the Health Protection Branch in February 1999, London Health Sciences Centre launched an effort to develop an acute stroke protocol (ASP).

Methods: Strategies to develop a coordinated response to acute stroke included: recruiting a stroke coordinator; organizing 24 hour stroke team coverage; developing evidence-based protocols and guidelines; approval by medical and pharmacy committees; implementing measures to reduce "average door to needle time" (ADNT); and case review. No coordinated paramedic or public education campaign was conducted.

Results: 24 stroke patients were treated with tPA between December 1998 and December 1999. Comparisons were made between the first and last 6 months: patients treated 4 vs. 20; ADNT (minutes), 108.5 vs. 93.8; average time to CT (minutes),

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67.0 vs. 53.2; average time CT to tPA (minutes), 41.5 vs. 38.4. Clinical outcomes are similar to the NINDS trial.

Conclusions: The changes implemented were followed by an improvement in recruitment and treatment times, in the absence of a paramedic or public education program. These changes cannot be specifically related to a single effort. We believe that a coordinated system for response to acute stroke is a critical component in developing an effective ASP with good patient outcomes.

J-08

Ten Years of Experience with Hemorrhagic Stroke in Young Adults

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Background: Hemorrhagic stroke accounts for 10% of strokes in all ages. However, in the young (between ages 15-45) the incidence is reported to be up to 40%. The most common etiologies include intracranial vascular malformation, aneurysms, arterial hypertension and abuse of illicit drugs.

Methods: The etiologies of stroke in the young who were admitted to the University of Alberta Hospital (UAH) from January 1, 1990, to December 31, 1999 were retrospectively reviewed. The results of cerebral angiogram, magnetic resonance angiogram, autopsy and risk factors were entered into a database.

Results: During this ten years, 93 hemorrhagic strokes in the young were identified of which 74 (52%) were male and 68 (48%) female. Subarachnoid hemorrhage (SAH) was diagnosed in 9 (9.7%) and intraparenchymal hemorrhage in 84 (90.3%) patients. Of the 84 intraparenchymal hemorrhages 42 (45%) were lobar, 27 (29%) deep brain and brain stem, and 9 (9.7%) isolated intraventricular hemorrhage. Of the 9 SAH, 2 died prior to angiogram, 4 were due to ruptured aneurysm, 1 was traumatic, 1 had arterial dissection, and 1 had no known cause. In the remaining patients 15 (16%) had vascular malformation, 16 (17.2%) arterial hypertension, 4 (4.3%) venous sinus thrombosis, 8 (8.6%) leukemia or lymphoma with critically low platelets, 4 (4.3%) brain tumour, and 20 (21.5%) abused alcohol, cocaine, or other drugs.

Conclusion: In our study of 235 strokes in the young, 93 (39.6%) had hemorrhagic strokes. This is in agreement with previous studies in the literature. Unlike the older adult patients with cerebral hemorrhage an etiology was evident in the majority of patients.

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POSTER PRESENTATIONS

SPINAL SURGERY

P-001

Intraoperative Urodynamic Monitoring for the Release of Tethered Cord Syndrome

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The tethered spinal cord presents potentially grave neurological and urologic implications. Presenting symptoms may include progressive spinal or lower limb deformity, back and leg pain, motor and sensory deficit of the lower limbs and progressive urinary and stool incontinence. Intraoperative monitoring of the spinal cord and nerve roots is an important surgical adjunct to assist in the complete untethering with preservation of neurological function. Although there are different methods of intraoperative monitoring previously evaluated, the value of intraoperative urodynamic monitoring has not been properly addressed. Since 1981, we have utilized intraoperative urodynamic monitoring extensively during 248 untethering procedures. The urologic history was retrospectively correlated with preoperative and postoperative urodyamic assessment of 210 consecutive dysraphic children. The mean age of our patients was 6 years (7 days to 18 years & 8 months). 105 (50%) patients reported to have preoperative bladder problems and 130 (61.9%) showed abnormal preoperative urodynamic studies. Intraoperative urodynamic monitoring was used to evaluate the viability of neural elements that required section during the untethering procedure. Grade I untethering was achieved in 226 (91.1%) procedures while only 22 (8.9%) had grade II using Killors grading system. Five patients (0.2%) reported dysuria post operatively and only one patient (0.4%) proved to have UTI. No other urinary complications were found. Intraoperative time was not significantly affected by the urodynamic monitoring procedure. Post operatively 119 patients (91.6%) urologically impaired children improved to a better class while 6 patients (8%) remained the same and only one patient (0.4%) worsened. 36 (17.1%) achieved normal voiding and 67 (31.9%) were capable of adequate spontaneous voiding and intermittent catheterization. None of the patients with normal urodynamic status had urologically changed.

Conclusion: Intraoperative urodynamic monitoring is a useful adjunct to improve the urologic outcomes of patients undergoing untethering of their spinal cords.

P-002

Outcome Analysis in Spinal Surgery; Has the Post-operative Clinical Examination Become Redundant?

E. Berger, (Montreal, Quebec).

Background: In recent years increasing attention has been focussed on outcome analysis using written and mailed questionnaires and/or telephone interviews.

Methods: A systematic search of published articles containing outcomes analyses based on questionnaires was made. Specifically, results obtained using the following research tools were considered: SIP (sickness impact profile), Roland-Morris disability questionnaire, Oswestry disability questionnaire, SF-36 (medical outcomes study short form 36-items health survey), Waddell disability index, Million visual analog scale, Dallas pain questionnaire, Quebec back pain disability scale, MSPQ (modified somatic perception questionnaire), Zung self-rating depression scale, Ransford's pain drawings, Stauffer and Coventry criteria, Beaujon's functional scale, Prolo score, LBOS (low back outcome scale) Greenough Frazer.

Results: Most of the studies relied on one or more of the above mentioned scales to establish post-operative results. Very few included a systematic post-operative clinical follow-up which in the rarest of cases was performed by independent observers.

Conclusions: While questionnaire responses in assessing post-operative results provide some information they cannot replace a thorough post-operative clinical examination and are practically useless in compensation or litigation cases.

P-003

Clinical and Radiological Evaluation of the Codman Semi-Constrained Load Sharing Anterior Cervical Plate: Results of a Prospective, Multicenter Trial with Independent, Blinded Evaluation of Outcome

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

We conducted a prospective multicenter study in 195 patients to evaluate the Codman semi-constrained plating system for anterior cervical fixation. This device allows dynamic change in the angle between the screws and the plate within the sagittal plane, allowing greater load sharing between host and graft bone in the event of graft resorption.

All patients underwent an anterior cervical fusion procedure employing the Codman plate. Clinical and radiological evaluation was performed at 1, 3, 6, 12 and 24 months. Follow-up compliance was 79.2% at 12 months and 52.6% at 24 months. A blinded independent observer evaluated radiographs for screw angles, construct height, fusion, hardware fracture and screw displacement.

We found a statistically significant change in the screw-plate angle, particularly during the first six months. A greater change occurred at the caudal screws (mean 7.8º) than at the rostral screws (mean 2.1º). The direction of change was compatible with graft resorption. The fusion rate was 93.8% at 24 months. Screw fractures were observed in five cases. Screw pullout was seen in nine cases. Five patients required re-operation for graft extrusion, one with an associated esophageal fistula.

We conclude that semi-constrained systems, such as the Codman plate, provide effective fixation with satisfactory load sharing.

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P-004

Neurologic and Urodynamic Outcome After Micro-surgical Release of Tethered Cord in Adults: Long Term Follow-up in 21 Consecutive Cases

Devanand A. Dominique, Sidney B. Radomski, Magdy Hassouna, Michael G. Fehlings (Toronto, Ontario)

Introduction: The appropriate timing of surgical intervention and neurological/urological outcome in adult patients with tethered cord syndrome remains uncertain. We report our surgical experience, with long term follow-up, in 21 consecutive adult patients (10 men and 11 women; ages 15 - 59) treated for the management of their tethered cord.

Methods/Results: All patients underwent formal pre- and post-operative urodynamic evaluation and intra-operative, SSEP, EMG, and urodynamic monitoring. The most common presenting complaint in our series was urinary/sexual dysfunction in 14 patients, followed by pain and weakness. Operative findings revealed 7 cases of split cord malformation and lipomyelomeningocele, 5 cases of fatty filum terminale, and 1 dermoid and 1 myelomeningocele. A mean post-operative follow-up of 40 months revealed subjective and functional improvement in 15 patients and the remainder clinically stabilized.

Discussion/Conclusion: In our experience, those patients with urinary dysfunction do not improve after surgical release. However, of the 14 patients who had urological and sexual dysfunction prior to surgery, >50% reported functional improvement, after micro-surgical release. We conclude that early micro-surgical release of a tethered cord may improve or at least inhibit neurologic deterioration. This procedure should be undertaken prior to the development of an overt neurogenic bladder.

P-005

Outcome Analysis of Surgical Options in the Treatment of Low Grade Lumbar Spondylolisthesis

F. Durity, R. Colistro (Vancouver, British Columbia)

Background: Controversy exists as to whether simple neural compression alone or added fusion is needed to relieve symptomatic low-grade lumbar spondylolisthesis (lgls) after failed conservative measures.

Methods: Over a two year period, 30 consecutive lgls patients (ages 32 - 71 years, median: 50 years) underwent posterior decompression. 21 underwent simultaneous attempted arthrodesis, with transpedicular screw fixation (N= 11), or intertransverse onlay graft (N= 10). Several factors including age, gender, degree of slip/stenosis, and solidness of fusion were correlated with outcome and patient satisfaction.

Results: >80% of patients with solid arthrodesis reported good to excellent outcomes (reduced pain, improved activity), compared to <20% satisfactory results in those with decompression only or failed fusions ($p<.001$). Screw fixation correlated highly with post-op successful arthrodesis ($p<.02$)) but for these patients hospital stay, however, was doubled (mean patient days: 7.8 days vs. 3.9 days).

Conclusions: In symptomatic lgls patients requiring surgery instrumented screw fixation achieves a high success rate for solid fusion and a good outcome at the small price of a longer hospital stay. No other patient factors were significantly correlated with a good result.

P-006

Dural Arteriovenous Fistula (DAVF) Simulating Spinal Cord Tumor on MRI: A Report of Two Cases

M. Goyal, R.A. Willinsky, K.G. terBrugge, W. Montanera, M. Tymianski (Toronto, Ontario)

Object: To present two cases of SDAVFs in whom MRI findings were suggestive of a spinal cord tumor leading to an inadvertent biopsy prior to the diagnostic angiogram.

Materials: Clinical, MRI and angiographic of two patients who presented with progressive cervical myelopathy and an MR diagnosis of spinal cord tumor was suggested, were reviewed. Both patients underwent an open biopsy and subsequently a conventional spinal angiogram.

Results: Both the patients had a gradual onset cervical myelopathy. MRI of the spine showed mild thickening of the cervicothoracic spinal cord with hyperintensity within it on T2-weighted images. No flow voids were seen within the subarachnoid space and the spinal cord-CSF interface was not fuzzy. In one patient there was patchy, irregular enhancement of the spinal cord on post contrast images. In both patients, a preoperative diagnosis of spinal cord tumor was considered and spinal DAVF was not entertained in the differential diagnosis. Both patients underwent an open biopsy, which was unremarkable. Subsequently, a conventional spinal (and cerebral in one patient) angiogram was performed which revealed a spinal DAVF at L3 level in one patient and a cranial DAVF at the level of the clivus (with arterial supply from the internal carotid artery and venous drainage caudally to the cervical perimedullary veins) in the other patient. Both patients were treated successfully by surgical clipping of the draining vein.

Conclusion: A high index of suspicion should be maintained for SDAVFs in patients presenting with gradual onset myelopathy with diffuse hyperintensity within the spinal cord on T2-weighted images even in the absence of flow voids in the subarachnoid space.

P-007

Are Psycho-Social Factors More Important than Anatomical Features in Predicting Outcome of Spine Surgery?

Z.H.T. Kiss, K. O'Rourke, J.B. Kelly (Ottawa, Ontario)

Background: Failed back surgery syndrome will develop in a proportion of patients undergoing lumbar spine surgery. The factors that predict failure in these patients are unknown, although many have been proposed. The only consistently reported factor is litigation or workman's compensation (WCB) involvement. This suggests that psychosocial factors are more relevant in predicting results of spinal surgery than anatomical abnormalities. The aim of this project is to predict which patients

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will fail spinal surgery in a poor prognostic group, the WCB population.

Methods: Using a retrospective cohort design, the Ontario WCB database of workers undergoing lumbar spinal surgery will be examined for prognostic indicators to answer the above research question. Success is defined as return to work or equivalent within 1 year of surgery. A group of surgical successes will be compared to a cohort group of failures for predictive factors; these include chronicity of pain, premorbid pain syndromes, Waddell signs, trigger points, neurologic findings matching radiology, operative technique, complications, surgical specialty, strategies employed to reduce epidural fibrosis, and post operative pain control. Data mining and classical multivariate statistical techniques will be used to determine the best predictors of this set.

Results: Preliminary data suggest that successful outcomes *do* occur in this population. Congruency of radiologic and neurologic findings are more likely associated with success.

Conclusions: No conclusions can yet be drawn. The power of this study rests in the following unique features: chart abstraction is used instead of administrative data, no patient is lost to follow-up, the database is on going so that a predictive model can be developed and then tested prospectively on other patients.

P-008

Occipitocervical Reconstruction with the Omi Loop: Results of a Multicentre Evaluation

M.G. Fehlings, S.K. Singh, L. Rickards (Toronto, Ontario), R. Apfelbaum (Salt Lake City, Utah), J. Hurlbert (Calgary, Alberta), D. Maiman (Milwaukee, Wisconsin).

Background: Reconstruction of the unstable craniocervical junction remains a major challenge. The benefits and downfalls of current methods of occipitocervical fusion are evaluated, and further compared and contrasted with a new precontoured occipitocervical fixation system, the OMI loop.

Methods: This retrospective, multicentre study reviews the records of 55 patients with craniocervical junction instability caused by rheumatoid arthritis (n=35), traumatic C1 or C2 fractures (n=11), tumour (n=1), and pseudoarthroses/other (n=4), who underwent occipitocervical reconstruction with the OMI loop.

Results: A solid reconstruction was achieved in all cases, with a post-operative stability rate of 100%. There were no neurological complications, and a 77.7% reduction in myelopathy and 65% reduction in neck pain were achieved post-operatively. Bony fusion was achieved in 86% of patients at minimum 3 months follow-up. Hardware failure occurred in 2 patients, infection in 5 patients, systemic perioperative morbidity in 7 patients and death in 2 patients.

Conclusions: The OMI Loop is a versatile, easy to use precontoured occipitocervical fusion device that can be applied to a wide range of craniocervical junction pathology, with a good post-operative neurological outcome. Our experience demonstrates a low rate of hardware failure coupled with a high rate of bony fusion and stability.

P-009

Sacro-iliac Fixation in Complex Lumbar Fusions

S. Sriharan, S. Chakravarthi, S. Brien (Windsor, Ontario)

Background: Sacroiliac fixation is a useful adjunct in thoracolumbar fusions. Its indications include: trauma of the lower lumbar spine where there is concurrent insufficiency of the pelvic girdle especially the SI joint; long thoracolumbar fusions extending to the lower lumbar spine; and neoplasm and tumors with involvement of the sacroiliac joints.

Methods: This can be achieved with either precontoured rods or using special iliac screws. We illustrate the indications, surgical principles, and techniques involved with this fixation method using two surgical cases.

Results: The first is a fifteen-year-old trauma patient with severe fracture/dislocation of the lumbar spine and sacroiliac joint. The second is a patient with neurofibromatosis Type I with multiple neurofibromas, numerous operations for kyphoscoliosis presenting with recurrent tumor and failure of previous instrumentation. In both these patients a stable fusion was achieved.

Conclusions: Fixation to the pelvis is therefore a useful technique in difficult or complex lumbar fusions.

P-010

Experimental Evaluation of Bradykinin Antagonist (CP-0597) in Acute Spinal Cord Injury (ASCI) in the Rat: Preliminary Report

P. Narotam, E. Massicotte, S. Weisner, R. Aitken, (Winnipeg, Manitoba)

Introduction: Kinin-Kallikrein system (KKS) is pivotal in the inflammatory response to tissue injury. Involvement of the KKS in experimental ASCI was demonstrated in 1989. CP0127, a specific bradykinin antagonist has been successfully used for traumatic brain injury. CP-0597, newer and 5 times more potent, was evaluated in experimental ASCI.

Methods: A randomized double blind placebo controlled study was conducted in adult rats (n=30). Following laminectomy at T12, a moderate injury was created using a dropped weight technique. CP-0597 or placebo was infused with a subcutaneous osmotic pump. Functional outcome was determined by using the Tarlov's Index (clinical outcome) and Inclined Plane Ability (withstand gravity) and compared (n=18).

Results: At 15 days, CP-0597 was favored over placebo in improvements in Tarlov Index Scores (5/9 vs. 3/9) and Inclined Plane activity (9/9 vs. 7/9). The median Tarlov's Index had improved from a baseline of 2 (moderate injury) to 3 (walking ability) with CP-0597 vs. no change in placebo. Median Inclined Plane activity for CP-0597 improved from 37 post injury to 47 at 15 days vs. 37 to 41 for placebo.

Conclusions: This preliminary study indicates that CP-0597 has potential in the management of ASCI. Further studies are being undertaken to confirm these findings and control variables more tightly.

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GENERAL NEUROSURGERY

P-011

Antesigmoid, Transtentorial Approach for Basilar Trunk Aneurysms

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Background: Basilar trunk aneurysms are uncommon lesions and difficult to treat by direct surgical methods. The endovascular approach, however, is not always feasible and surgery may be the sole treatment possible.

Methods: We reviewed a series of 4 consecutives patients admitted for a ruptured basilar trunk aneurysm and approached by an antesigmoid transtentorial route.

Results: Two patients were in H & H grade III and 2 patients in grade II before surgery. All aneurysms were clipped. There was no mortality. All patients had a good to excellent outcome with transient sixth cranial nerve paresis in 2 cases.

Conclusions: Antesigmoid, transtentorial approach offers an excellent route for basilar trunk aneurysm. The relevant surgical technique and anatomy will be emphasized.

P-012

Radiosurgery vs. Surgical Resection for the Treatment of Cerebral Metastasis: A Systematic Review

J.D. Atkinson, J. Golan, J.L. Caron (Montreal, Quebec)

Background: For many years now, radiosurgery has offered an alternative to resection in patients with cerebral metastases. Unfortunately, published reports have consisted mostly of scattered case and cohort studies, with little careful unbiased analysis of outcome. In this report we review the literature supporting the radiosurgical treatment of brain metastases.

Methods: We performed a systematic review of the English literature on radiosurgery for brain metastases. The Medline data base from 1988 to the present was searched using keywords radiosurgery, metastases, brain tumours. Additional references were located using the bibliography list of selected papers.

Results: Of a total of 88, 28 reports were selected to be consistent with the objective of the review. No randomized control trials have been performed on this subject, and all but 3 of the studies were descriptive or case series. 1762 patients and > 2550 lesions are described with a combined median survival of 8 months and local recurrence rate of approximately 13%. Characteristics associated with better outcome included age (< 60 years old), less than three metastatic lesions, tumour diameter <3 cm, KPS score >70, and the absence of systemic disease. The influence of tumour pathology is uncertain.

Conclusions: Surgical treatment for single brain metastases has been established with two randomized control trials comparing surgery to WBRT alone. From the available literature radiosurgery appears to have efficacy rates in the general range of surgical therapy. Unfortunately conflicting results in cohort trials and the lack of carefully controlled studies make the role of radiosurgery in comparison to other treatment modalities uncertain.

P-013

An Innovative Curriculum Plan: Death and Dying in Neurosurgery

S. Brien, (Windsor, Ontario)

Background: The Royal College of Physicians and Surgeons (RCPSC) have determined that with respect to attitudes and deportment, the resident will demonstrate: *a sympathetic understanding of human dignity, weaknesses and intolerance's as revealed by compassion to patients and their families, particular in the circumstances of death and dying*. Knowledge, skills and attitudes can not be taught separately, but must be merged to be an integral component of learning schemes and not just taught as an isolated course. The goal of this project was to develop an innovative curriculum that provides a framework for residents and training directors to explore one of the professional attitude objectives outlined by the RCPSC.

Methods: The curriculum is case-based. A collection of teaching modules was created to integrate several issues from various learning domains. Learning methods include action learning circles (Wade and Hammick, 1999) and the use of reflective journals (Schon, 1983). Formal reflections would be encouraged in an e-journal that would facilitate debriefing of critical incidents, reflect on standard cases and help evaluate the course content.

Conclusions: In keeping with the quest of the CanMEDS 2000 project, professional roles must be nurtured and integrated into the Neurosurgery training program. The methods, although not novel in medical education, are still unique in surgical training.

P-014

Strategies for Community Neurosurgeons to Maintain Certification

S. Brien, (Windsor, Ontario)

Background: With the advent of the millennium comes the initiation of mandatory maintenance of certification for Canadian subspecialists. Surgeons practicing outside the University centers must devise a creative educational plan in order to implement and document ongoing professional activities. The frame work of Continued Professional Development (CPD) as designed by the RCPSC requires fellows to earn 400 credits over five years. The sections include accredited group activities, other learning activities, accredited self-assessment programs, structured learning projects, practice review and appraisal, educational development, teaching and research.

Methods: The Kolb's Learning Style Inventory was used by members of the Department of Neurosurgery to determine their own learning style. This information was useful to create individual and group learning outcomes using the CPD guidelines. Local learning resources were evaluated.

Results: The plan devised was multi-layered. Steps included documenting weekly meetings case discussion by the neurosurgeon on call, yearly planning of CME meeting attendance, methods of personal and group documentation

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designed as an "education" card. Office software and hardware were updated to include e-mail, intra and internet access to facilitate on-line teaching opportunities. The Kolb inventory allowed the identification of physician's learning styles which was then matched to CPD activities to encourage a self-directed learner-centered plan.

Conclusions: The stepwise strategic plan to maintain certification by one group of community neurosurgeons will be discussed.

P-015

The Role for Nonsurgical Cranial Remodeling in a Comprehensive Craniofacial Program

M.G. Hamilton, S.T. Myles, D. McPhalen (Calgary, Alberta)

Occipital positional (deformational) plagiocephaly is by far the most common craniofacial or head shape problem seen by a pediatric neurosurgeon. Occipital positional plagiocephaly does not correct spontaneously. Aggressive repositioning efforts can correct a significant amount of the deformity in many infants if initiated early. However, the management of more severe positional plagiocephaly, or when repositioning efforts are started too late to be effective is more complicated. Most Canadian craniofacial centers unfortunately have no nonsurgical option available for treatment of significant positional plagiocephaly. We have initiated the "Alberta Infant Cranial Remodeling Program" to provide nonsurgical cranial remodeling treatment for positional plagiocephaly utilizing the Dynamic Orthotic Cranioplasty (D.O.C.) headband. We have assessed over 800 children and treated 165 with the D.O.C. headband during the past three years. All patients treated with the D.O.C. headband have been followed with photos, anthropometric measurements, and clinical evaluation. Treatment results have demonstrated effective correction of deformational head shapes. There has been no morbidity in this patient population. Nonsurgical techniques for correction of positional plagiocephaly are an essential part of a comprehensive craniofacial program and should be available in all pediatric neurosurgical centers.

P-016

The Successful Integration of Frameless Stereotaxy with the Mobile 1.5-Tesla Intraoperative MR Imaging System

M.G. Hamilton, J. Vecil, T. Kaibara and G.R. Sutherland (Calgary, Alberta)

We have previously reported the development of a moveable, high field intraoperative magnetic resonance (MR) imaging system for neurosurgery. The magnet is moved into and out of the surgical field to acquire high-definition MR images. This system has been used in over 90 neurosurgical procedures. We report the successful integration of the Brain Lab image-guided navigational system with the intraoperative MR system. MR images are acquired with the patient positioned in an MR-compatible 3-pin head holder with a unique fiducial system. Data is transferred to the VectorVision2 Brain Lab system and registration and navigation is performed. Interdissection MR images are utilized to update navigational data during surgery as preoperative data rapidly becomes obsolete as brainshift occurs secondary to the effects of surgery (CSF aspiration, tumor excision, etc).

We have utilized this system in three patients undergoing brain tumor surgery. All patients had successful initial registration with an average accuracy of approximately 2.0 mm. Interdissection MR imaging with updated registration was undertaken in 2 patients with a similar accuracy.

The integration of an image-guided system into a high field intraoperative MR system provides a tremendous advance in intraoperative frameless navigation. With improvements to the fixation of intraoperative registration markers, we expect significant improvement in registration accuracy.

P-017

A Comparison of Dural Closures using Suture, Fibrin Adhesive (Tisseel) and Surgicel in an *In Vitro* Model

J.F. Megyesi, E. Kachur, W. MacDonald, R.F. Del Maestro (London, Ontario)

Background: The watertight reapproximation of the dura mater is fundamental to intracranial procedures. To this end, a number of materials have been used including suture, fibrin adhesive (Tisseel), Surgicel or a combination. Using a previously described laboratory model that allows us to measure leak pressures, we have compared the reapproximation of dural openings using various techniques.

Methods: One cm dural incisions and 2 cm dural incisions were reapproximated using various combinations of suture, fibrin adhesive and Surgicel and the leak pressures compared. One cm x 3 cm dural windows were closed with commercially available cadaveric dura and various combinations of suture, fibrin adhesive and Surgicel and the leak pressures compared.

Results: The pressure at which 1 cm linear dural incisions leaked was significantly higher when closed with fibrin adhesive and Surgicel ($P < 0.05$). The pressure at which 2 cm linear dural incisions leaked was significantly higher when closed with suture followed by fibrin adhesive ($P < 0.05$) The pressure at which 1 cm x 3 cm duraplasties leaked was significantly higher when closed with suture followed by fibrin adhesive ($P < 0.05$).

Conclusions: The watertight reapproximation of small dural incisions, especially when hard to suture, may by accomplished with fibrin adhesive and Surgicel. The watertight reapproximation of large dural incisions and duraplasties, especially those located in places prone to cerebrospinal fluid leakage, is best done with suture followed by fibrin adhesive.

P-018

Needs Assessment for Neurosurgical Residency Education

K.D. McReelis, M.D. Cusimano (Toronto, Ontario)

Background: Numerous challenges are facing residency education today. These include financial and human resource stresses in addition to educational requirements from certification bodies. We have undertaken an extensive

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assessment of key stakeholders in this process to better assess learning needs for trainees and to identify key areas for improvement in neurosurgery education so as to better reflect current practice needs.

Methods: Information from key stakeholders was collected including residents and faculty, professional associations and provincial health plan data. Strategies included written needs assessment survey with focus group discussions coupled to data collection from identified stakeholders.

Results: Goals and objectives of the program remain high in the opinions of all concerned. Assessment information revealed need for enhanced coverage in the areas of applied neuroanatomy, basic science coverage, principles of evidence based practice and introduction of elements of professional practice including medico-legal issues. Data was also collected on the relative importance of subject topics to be used for curriculum planning.

Conclusion: Needs assessment of key stakeholders for a neurosurgery residency program identified several areas for improvement that can be used to build an improved curriculum. These results have wide based applicability for other residency programs across Canada.

P-019

Communicating Hydrocephalus and Vestibular Schwannomas: Etiological Considerations

M. Stoffman, R. Leblanc, D. Melanson, A. Zeitouni, (Montreal, Canada)

Background: We report the occurrence of symptomatic communicating hydrocephalus in 5 patients with small vestibular Schwannomas (VS).

Methods: A retrospective review of patients with a VS was performed addressing clinical presentation, radiological features, treatment, outcome and CSF biochemistry.

Results: Two males and three females aged 44-77 years had cognitive alterations and ataxic gait characteristic of normal pressure hydrocephalus and radiologically-demonstrated communicating hydrocephalus with a small (2-2.3 cm) VS. The CSF protein was elevated (0.64-0.92 g/L, normal 0.2-0.5 g/L) in all cases. The VS was resected in 3 patients but they still required ventriculo-peritoneal (VP) shunting for symptomatic relief. VP shunting alone relieved the symptoms in the other 2 patients.

Conclusions: The tumors in our cases were not large enough to obstruct the ventricular system. We therefore postulate that the clinical presentation of our patients resulted from interference with CSF absorption at the level of the arachnoid granulations caused by the high protein content of the CSF. Removal of the tumor did not result in the radiological resolution of the hydrocephalus or in clinical improvement which were only achieved by VP shunting. It is not necessary to treat small vestibular Schwannomas (VS) to alleviate communicating hydrocephalus as this can be accomplished by VP shunting alone.

P-020

Collagen Matrix (Duragen) for Duraplasty Following Cranial and Spinal Surgery

P. Narotam, A. Gousseau, G. McGinn (Winnipeg, Manitoba)

Introduction: Neurosurgeons frequently need to use dural grafts when primary closure cannot be achieved due to dural retraction and shrinkage. Dural closure is still controversial. Previously, "watertight" dural closure has been advocated. Recent extensive clinical experience with collagen sponge has shown superior healing properties.

Methodology: A retrospective clinical study was conducted using a newer collagen matrix as an onlay dural graft. Graft failure i.e. CSF leakage from the incision or wound sepsis attributed to the graft was determined. Secondary endpoints were delayed hemorrhages or subgaleal fluid collections. Hydrocephalus was monitored as a co-morbidity. MRI scans were examined (n=40) for complications. Histology was performed (n=20) at autopsy or from re-operations.

Results: Over a 4-year period (1996-1999), 380 patients were evaluated. The collagen matrix had an extremely low failure rate (<5%). There was no increase in wound sepsis. At MRI, no abnormal enhancement was seen. As seen from histology, the matrix provided a 3D structure for dural repair.

Conclusions: Collagen matrix is easy to use, safe and effective for duraplasty. However, it must be used cautiously at the cranial base.

P-021

"Intact Brain Dead Patient!": A Sad Legacy of Cerebral Contusions

P. Narotam (Winnipeg, Manitoba), N. Nathoo, P. Govender, J.R. van Dellen (Durban, South Africa)

Background: Patients with focal post-traumatic brain contusions often present to hospital with high GCS. Surgeons have been reluctant to evacuate contusions for fear of removing potentially viable brain. This has often led to unexpected deaths with reported mortality rates of 30-40%. In a 15 year study involving > 1500 patients with focal contusions, we report on the efficacy of various treatment modalities i.e. observation, ICPM with medical therapy or surgery.

Methods: A retrospective analysis of contusion management was undertaken from 1983 to 1987. Its effect on mortality was compared to management mortality for trauma. From this experience, a contusion management protocol was devised (1987) and implemented from 1988 onwards. The effectiveness of the "protocol" was validated prospectively by examining its impact on contusion mortality.

Results: Pre-protocol: During 1983-4, contusion mortality of 23-35% and a trauma mortality of 20-25% was found. In 1985-6, ICPMs were placed to determine the "at risk" patients. 30% developed RICP. The mortality during this period dropped to 12.5%. Protocol Era: Implementation of clinical and radiological criteria for contusion management was effective in reducing the mortality to 2-5%.

Conclusions: The implementation of a management protocol

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using well defined clinical and CT criteria have removed the unpredictability in treating these treacherous lesions.

P-022

Cortical and Ependymal Closure with the Fibrin Adhesive, Tisseel: Reoperation and Pathology of the Resulting Fibrin Membranes

R.F. Del Maestro, (London, Ontario)

Background: The transcortical resection of intraventricular and/or paraventricular tumors is frequently associated with the development of subdural fluid collections. The use of fibrin adhesive, Tisseel to seal cortical and ependymal defects after these procedures appears to prevent the development of subdural collections. This study was carried out to assess the surgical difficulties in reopening previously closed cortical and ependymal defects when carrying out repeat operations and to outline the pathology of the fibrin membranes which result from the use of Tisseel.

Methods: The records of 38 consecutive patients who underwent 45 operative procedures from 1994-1999 in which Tisseel was used to close cortical (35 operations, 78%} ependymal defects (9) or both (1) were reviewed.

Results: In 6 patients 7 repeat operations were carried out through 4 previously closed cortical defects and 3 operations through 2 previously closed ependymal defects. A thickened opaque arachnoid-like membrane was found covering the cortical and ependymal defects in each case. This membrane was not adherent to overlying dura and appeared not to allow the passage of CSF. It was not difficult to excise the central portion of the membrane and reenter the ventricle. These reopened cortical and ependymal surfaces were closed again without difficulty using Tisseel. Pathologically at two months, fibroblasts had invaded the fibrin mesh and collagen deposition was seen. An inflammatory and angiogenesis response was also evident. At nine months little inflammation was seen, angiogenesis appeared in the region of the previous fibrin seal and a well developed collagen network was visualized.

Conclusions: The use of the fibrin adhesive, Tisseel, results in a permanent watertight collagen containing membrane over sealed cortical and ependymal defects. The resultant membranes may be readily opened for repeat operation and sealed again with tissue adhesive.

P-023

The Application of Image-Guided Neurosurgical Techniques in a Pediatric Population: A Preliminary Experience

A. Ranger, E.C.G. Ventureyra, M. Vassilyadi (Ottawa, Ontario)

Background: Frameless stereotaxy has evolved as an important means of increasing the safety and efficacy for a variety of neurosurgical procedures, but the applicability of this modality to procedures in infants and children has not been extensively documented and it remains a relatively new adjunct to pediatric neurosurgery. We report our preliminary experience with the use of frameless stereotaxy, applied to pediatric cases with diverse pathologies, utilizing a variety of surgical approaches.

Methods: Cases of children undergoing neurosurgical procedures with image-guidance at the Children's Hospital of Eastern Ontario were analysed retrospectively. From 1997 to the present, 22 frameless stereotactic procedures were performed in 21 patients (14 males, 7 females; mean age 8.8 years, range 3 weeks-22 years) for tumor surgery (including cerebral hemisphere, hypothalamus, posterior fossa, brainstem, pineal and optic-hypothalamic locations), cavernous hemangioma removal (hemispheric and brainstem locations), cortical dysplasia, hypothalamic and olfactory hamartomas, slit ventricle syndrome and corpus callosotomy for epilepsy. Surgery was performed with the Zeiss IGS System in all but two cases, in which the Stealth Navigator was employed. Skin fiducials and standard imaging protocols (2mm cranial CT and 2mm high resolution MRI) were used for surgical planning. Anesthetic and operative times were noted, with comparison made between cases of corpus callosotomy with and without image-guidance for these parameters.

Conclusion: The main advantages of neuronavigation relate to planning a safe corridor to brain lesions, with reliable lesion targeting. This technique adds an average of 111 minutes of anesthetic time to each case and, in corpus callosotomy, had no impact on operative time. No anesthetic complications were encountered. Special concerns exist for children, such as the need for prolonged anesthesia for preoperative image-acquisition and intraoperative head immobilization without the use of pins. We report our experience with this technique and have found it to be extremely versatile in planning and performing a number of different procedures in children, for pathologies ranging from tumors to intractable seizures or the slit-ventricle syndrome.

CEREBROVASCULAR DISEASE

P-024

Clinical Value of Contrast Agents in Transcranial Imaging

V. Beletsky, D. Brodie, P. Hamilton, J. Norris (Toronto, Ontario), O. Lagoda (Moscow, Russia)

Background: Transcranial Imaging (TCI) is a non-invasive ultrasonographic assessment of the intracranial circulation, identifying stenoses or potential sources of emboli apart from cardiac and extracranial carotid vessels. However, in about 20% of cases technical problems restrict its value. New contrast techniques have overcome this problem by an enhanced visualization of the intracranial circulation.

Methods: Using the IV contrast agent "Levovist" we have applied this technique in 38 patients with TIAor ischemic stroke, comparing the results to standard or MR angiography. We defined insonation "failure" as either failure to penetrate the temporal window or failure to insonate all segments of major intracranial arteries.

Results: In 20 patients (53%) TCI was deemed unsatisfactory for a variety of reasons, but with contrast, only 3 (8%) were inadequate for clinical decision-making. In 2 patients false-

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positive ACA and in one patient false-positive MCA stenoses were found after contrast.

Conclusions: Our data is probably distorted by referral bias, since the patients were specially selected for contrast studies. Nevertheless, contrast TCI is a valuable addition in excluding intracranial stenoses and occlusions, which is especially important when considering carotid endarterectomy.

P-025

Cognitive Effect of Intracranial Microemboli in Patients with Mechanical Heart Valves

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

Background: Prosthetic heart valves may cause cognitive impairment by generating microemboli detected by Transcranial Doppler monitoring.

Methods: Patients with mechanical valves were divided into asymptomatic and symptomatic (TIAand stroke) groups. All had bilateral 30-minute MCA monitoring for microemboli (HITS) with and without oxygen inhalation and had selective cognitive testing (including MMSE, Microcog, WAIS-III and Dementia Rating scores). All symptomatic patients had CTor MRI scanning.

Results: There were 36 patients, 20 with mitral, 9 with aortic and 7 with combined valves, mean age 58±13 years. In the asymptomatic group (22 patients) HITS frequency was 23.5±30.2 before oxygen inhalation and 4.0±9.7 after. In the symptomatic group (16 patients) these figures were 19.0±32.and 3.0±8.4 correspondingly. Cognitive testing showed no differences between the groups.

Conclusions: Oxygen inhalation during TCD monitoring is clearly critical for proper interpretation the relationship of HITS to cognitive impairment. The lack of detectable effect of HITS on cognitive function may be due to the high incidence of gaseous bubbles, generated by valve motion rather than particulate emboli. Further studies should focus on patients with persisting high HITS rate after oxygen inhalation.

P-026

Stroke Following Lung Transplantation: A Case Report and Review of the Literature

K.M. Chapman, P.A. Teal (Vancouver, British Columbia)

Background: Stroke is a rare complication following lung transplantation. To our knowledge there are 7 reported cases in the literature, and the differential diagnosis has not been systematically reviewed. The number of lung transplants is increasing; to date, over 650 lung transplants have been done in Canada.

Methods: Case report and review of the literature.

Results: A 40-year-old woman with cystic fibrosis underwent bilateral lung transplantation for end stage disease. Following a focal seizure, neurological examination revealed right sensorimotor deficits. Stroke risk factors included diabetes and a positive family history of stroke. Cyclosporine level was supratherapeutic.

A definitive diagnosis was not established, but potential transplant-related stroke mechanisms including pulmonary venous thrombosis at the surgical anastamosis, immunosuppression (angioinvasive infections, endocarditis), drug effect - particularly cyclosporine, venous sinus thrombosis, and hypercoagulable state are discussed.

The utility of transthoracic/transesophageal echocardiogram, spiral CT, and angiogram in the diagnosis of pulmonary vein thrombus, and management of stroke post lung transplant are reviewed.

Conclusions: This case illustrates the diagnostic and management challenges in stroke following lung transplant. Physicians should be aware of specific transplant-related stroke etiologies.

P-027

The Effect of Carotid Endarterectomy on the Cerebrovascular Reserve: Study of Fifteen Symptomatic Patients

D. Charest, P. Couillard, G. Lamoureux (Sherbrooke, Quebec)

The cerebrovascular reserve can be assessed with cerebral blood flow studies (PET, SPECT, Xe-CT) and is defined as an impaired response to intravenous acetazolamide. We studied fifteen consecutive patients undergoing carotid endarterectomy for a symptomatic, greater than 70% stenosis. All patients were evaluated by preoperative, early postoperative (48 h.) and late postoperative (6-8 weeks) SPECT studies with acetazolamide challenge. One third of our patients had an abnormal cerebrovascular reserve preoperatively. All the abnormal preoperative studies were corrected in the late postoperative period. The early postoperative studies showed a globally decreased captation in all our cases. Carotid endartectomy therefore corrects both the emboligenic and hemodynamic aspects of a symptomatic stenosis.

P-028

The Spectrum of Cerebral Ischemia in Oral Contraceptive Users

Seemant Chaturvedi (Detroit, Michigan)

Background: Previous epidemiologic studies have shown a slightly increased risk for ischemic stroke in women who use oral contraceptives (OCPs). Cigarette smoking, hypertension, and age greater than 35 have been suggested to be additional risk factors. Detailed stroke mechanisms in individual patients are less well defined.

Methods: Case series from the stroke clinic of a University medical center.

Results: Eight women were identified with stroke (seven) or transient ischemic attack (one) over a four year period. The mean age of the patients was 33.9 years. Cigarette use was present in 50% but hypertension was present in only one patient (12.5%). In terms of stroke mechanism, three patients had a patent foramen ovale (PFO) and were classified as cardioembolic. One patient had an arterial dissection. One patient had livedo

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reticularis and possible Sneddon's syndrome. Another woman had angiographic evidence of fibromuscular dysplasia. The remaining two patients had migraine headache in addition to OCP use.

Conclusions: Women with cerebral ischemia while taking OCPs can have a variety of coexisting pathologies and stroke mechanisms. Transesophageal echocardiography should be undertaken in these patients to check for PFO. Arterial disorders and a history of migraine should also be investigated.

P-029

Possible Role of Protein Mono-ADP-Ribosylation in Oxidative Stress and Neurodegeneration in *In Vitro* Ischemia

M.V. Frantseva, P. L. Carlen, J. L. Perez Velazquez (Toronto, Ontario).

Background: Biochemical cascades triggered by ischemic injury cause mitochondrial dysfunction, termed mitochondrial permeability transition (MPT), previously observed in our ischemia model. We hypothesized that mitochondrial dysfunction and mono-ADP-ribosylation (mADPR) contributes to free radical (FR) production and neurodegeneration in neurons subjected to ischemic injury.

Methods: Ischemic insult was reproduced by superfusing organotypic hippocampal cultures with glucose-free deoxygenated medium. FR generation, mitochondrial calcium concentrations and cell death were assessed with fluorescence emission of dihydrorhodamine123, Rhod-2 and propidium iodide respectively. Neuronal membrane potential and input resistance were measured by whole-cell recordings.

Results: Ischemia-induced FR formation was decreased by the mitochondrial complex I blocker roteneone and paralleled mitochondrial calcium accumulation. The MPT blocker, CsA, completely prevented FR generation, significantly reduced mitochondrial calcium overload and prevented neuronal depolarization and input resistance decrease. A blocker of NAD^+ hydrolysis, nicotinamide, and an inhibitor of protein mono-ADP-ribosylation, MIBG, reproduced CsA effects on FR generation and mitochondrial calcium accumulation. Nicotinamide, CsA and MIBG significantly reduced neuronal loss caused by ischemia.

Conclusions: Our study suggests that NAD^+ hydrolysis and protein mono-ADP-ribosylation contribute to mitochondrial FR generation, impairment of mitochondrial calcium homeostasis and neurodegeneration caused by an ischemic insult.

P-030

The Management of Dyslipidemia in Ischemic Stroke and TIA Patients

T. Hall, M. Roy, C. Corman, A. Douen (Ottawa, Ontario)

Background: Several factors, including medical conditions, genetics and choice of lifestyles have been identified as risk factors for stroke. Dyslipidemia has been identified as one of these factors and recent studies involving the use of hydroxymethylglutaryl coenzyme A reductase inhibitors have demonstrated beneficial effects on both stroke and total mortality. The objective of this study was to assess the management of dyslipidemia in patients with ischemic stroke and transient ischemic attack (TIA) at a tertiary care hospital, the Ottawa Hospital, General Campus.

Methods: A retrospective chart review was conducted of patients diagnosed with TIA and/or ischemic stroke in 1998. Management of dyslipidemia was deemed necessary if the low density lipoprotein cholesterol level was ≥3.5 mmol/L or the total cholesterol to high density lipoprotein cholesterol ratio was > 5 upon request of a fasting lipid profile.

Results: Two hundred-and-eighty patients were identified of which 14.6% were receiving a lipid-lowering agent prior to admission. A lipid profile was ordered on admission for 62 patients of the remaining 239. Thirty-nine of the lipid profiles ordered were requested in a fasted state. Sixteen of the 39 were abnormal and only 5 of these patients were ordered a lipid-lowering agent. Another one of the 16 patients was recommended follow-up with the family physician after discharge. The remaining 10 were not managed.

Conclusion: Results from this study indicate that TIA/ stroke patients are seldom screened with a fasting lipid profile and those with documented dyslipidemia are not proactively managed.

P-031

Radiologic and Histopathologic Evaluation Using Guglielmi or Mechanically Detachable Platinum Coils in the Treatment of Sidewall Carotid Aneurysms in Swine

S.P. Lownie, R. Hammond, D. Pelz, L. Denning, B. Lehrbass (London, Ontario), D. Rosso, (Mississauga, Ontario)

Background: Controversy exists regarding the importance of electrothrombosis in aneurysm treatment. We evaluated the relative role of electrothrombosis compared to mechanically detachable (IDC) coils.

Methods: Sidewall aneurysms were created in swine. Embolization was performed after 1 week using GDC or IDC coils. Angiography was done 1 week post-embolization. Radiologic and pathological assessment was blinded. Aneurysm thrombosis was classified as 3+ (greater than 50%), 2+ (10-50%), 1+ (up to 10%) or 0 (none). Leukocyte density around the coils was categorized using a four point scale.

Results: Five animals died (3 from aneurysm rupture). Four aneurysms spontaneously thrombosed. 14 aneurysms were coiled (7 GDC, 7 IDC). In both groups, immediate angiography showed neck remnants and/or flow through coil interstices (11/14, 79%). At follow-up, 75% showed complete occlusion. Pathology showed almost half had no endothelial covering at the aneurysm neck. Fibroblast ingrowth was prominent at the dome periphery, less mature centrally. There was no difference between GDC and IDC coils. However, there was a tendency to greater clot organization with GDC compared to IDC coils. Leukocyte density was more pronounced around GDC versus IDC coils.

Conclusion: Complete neck endothelialization was the same in both groups. GDC aneurysms showed a greater tendency to early fibroblast ingrowth.

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P-032

Stent Angioplasty of Traumatic Superior Sagittal Sinus Occlusion

S.P. Lownie, R.L. Sahjpaul (London, Ontario)

Background: We report a case of superior sagittal sinus occlusion due to depressed skull fracture in which flow was restored using a self-expanding endovascular stent.

Methods: A 17-year-old male sustained an open depressed occipital skull fracture with an occipital hematoma. He deteriorated neurologically but at craniotomy the depressed fragment had torn and compressed the superior sagittal sinus and could not be elevated due to hemorrhage from the sinus. MRI showed thrombosis of the sinus due to occlusion by the depressed fragment. The sinus was cannulated via a burr hole placed anteriorly and a self expanding stent was introduced.

Results: Flow was restored in the sinus and the thrombosis cleared. Mild residual stenosis was seen due to the depressed fragment. Despite technical success the patient succumbed to diffuse cerebral edema. Autopsy showed optimal stent placement and the sinus was patent.

Conclusion: This case illustrates the technical feasibility of endovascular stenting of the superior sagittal sinus.

P-033

Organized Stroke Care Validated in a Canadian Teaching Hospital.

S Phillips, G Eskes, G Gubitz (Halifax, Nova Scotia)

Introduction: According to randomised data from stroke units in western Europe, organized care following stroke saves lives and reduces disability. Only a small number of Canadian hospitals have organized stroke care. We provide such care in our urban tertiary care teaching hospital, and present an audit of our performance.

Methods and Results: Patients with acute stroke are admitted to our 28 bed Stroke Service, which provides rapid evaluation, interventions, interdisciplinary functional assessments and early rehabilitation. Patient and family education is provided through structured family meetings. Advances in care are facilitated through educational workshops and ongoing clinical research. Prospective information about patient care is maintained on a computerized database. The 1997 in-hospital case-fatality rate was 10.6%, stroke progression/recurrence occurred in 4.5% of patients, pneumonia in 2.3% and non-fatal bleeding in 1.6%, all comparable to published rates. During hospitalization, most patients improved functionally, with significant increases in Barthel Index scores. Most patients went home; length of stay was dependent on stroke severity (median 6 days for mild strokes, 15 for moderate, and 26 for severe).

Conclusions: Organized stroke care in our hospital results in outcomes similar to published (European) data. This information may be useful for other acute care hospitals in Canada.

P-034

Etiology of Stroke in the Young: A Decade of Experience

M. Sazgar, M. Muratoglu, A. Shuaib (Edmonton, Alberta)

Background: The epidemiology of stroke in the young (age between 15 to 45) is relatively underreported in the literature. Studying the stroke in the young may help to better demonstrate the diverse and potentially preventable or treatable etiologies. It is possible that as a group young stroke sufferers have more treatable causes for stroke as compared to the older population.

Methods: Chart reviews were done in patients between ages 15-45 admitted with acute ischemic stroke to the University of Alberta Hospital (UAH) from January 1, 1990 to December 31, 1999. The etiology of stroke was scored based on "TOAST" classification.

Results: Ischemic stroke in the young was diagnosed in 142 patients. Of those 74 (52%) were male and 64 (48%) were female. Thirty-one (21.8%) had cardioembolic stroke, 2 (1.4%) had large artery atherosclerosis, 10 (7%) had small vessel disease and in 44 (31%) the etiology was unknown. Fifty-five (38.7%) cases had other known causes such as craniocervical arterial dissection 17 (12%), vasculitis 4 (2.8%), connective tissue disease and antiphospholipid antibody syndrome 16 (11.3%), hypercoagulable states, hematologic abnormalities and other etiologies.

Conclusion: Our experience with a large number of young patients shows that the commonest causes of stroke in the young include cardioembolic stroke, arterial dissection, and collagen vascular disease. Cervical atherosclerosis was seen in only 2 patients. It is important to aggressively investigate the etiology of stroke in the young, as the treatment options may be different from the older population.

P-035

Risk Factors in the Young with Stroke

M. Sazgar, M. Muratoglu, A. Shuaib (Edmonton, Alberta)

Background: Identifying risk factors is an important step in stroke prevention. In the young (ages between 15 to 45) connective tissue disorders, drug and alcohol abuse, migraine, smoking, hypertension, diabetes and possibly hyperlipidemia are among stroke risk factors.

Methods: The risk factors for stroke in the young who were admitted to the University of Alberta Hospital (UAH) from January 1, 1990, to December 31, 1999 were retrospectively reviewed and the results were entered into a database.

Results: During the above ten-year period there were 235 strokes in the young of which 142 (60.4%) were ischemic and 93 (39.6%) hemorrhagic. Of the total cases, 109 (46%) were female, and 126 (54%) male. Hypertension requiring treatment was seen in 71 (30%) patients. Twenty–three (9.8%) patients had diabetes mellitus and 55(23.4%) hyperlipidemia. One hundred and seventeen (50%) patients were smokers. Family history of premature coronary artery disease or cerebrovascular disease in the first degree relatives was present in 66 (28%) patients. History of alcoholism was present in 34 patients (14.5%), and history of illicit drug abuse in 29 (12.3%) patients. In 89 patients

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hypercoagulable work up was done. Of those 16 (6.8%) had elevated antiphospholipid antibody titre. Three patients were heterozygote for factor V Leiden mutation. Migraine history was recorded in 27 (11.5%) patients and 22 (9.4%) were on oral contraceptives.

Conclusion: Our findings indicate that most of the strokes in the young occur in patients with potentially modifiable risk factors such as hypertension, hyperlipidemia, and smoking. Stroke prevention strategies in the young should focus in aggressive management of modifiable risk factors.

P-036

Embolization of Small (< 3 cm) Brain Arteriovenous Malformations (AVMs): The Toronto Western Hospital Experience (1984 - 1999)

R.A. Willinsky, M. Goyal, K. terBrugge, W. Montanera (Toronto, Ontario)

Object: To review our results of embolization in < 3cm brain AVMs and test a grading system based on the angioarchitecture that would predict percentage obliteration.

Methods: 80 consecutive patients with < 3 cm brain AVMs were treated by embolization from 1984 to March 1999. The angioarchitecture of the AVMs were given a score from 0 to 6 based on the following features: nidus (fistula = 0, < 1 cm = 1, 1-3 cm = 2), arterial supply (cortical = 0, perforator = 1) (single = 0, multiple = 2), and venous drainage (single = 0, multiple = 1). Angiographic results were grouped into 3 categories based on percentage obliteration: complete, 66-99% and 0-65%.

Results: Embolization achieved complete obliteration in 22 of the 81 (27%) AVMs. Embolization was successful in eliminating pre-nidal aneurysms in 5 patients. In the 28 AVMs where the goal of embolization was cure, 19 (68%) were completely obliterated. In the 14 AVMs with angioarchitecture scores of 0-2, 12 (86%) were cured. In the 23 AVMs with scores of 3-4, 8 (34%) were cured. In the 44 AVMs with scores of 5-6, 2 (4%) were cured. Embolization resulted in a permanent morbidity of 1.3% and a mortality of 1.3%.

Conclusions: Embolization is an effective treatment of < 3 cm AVMs when the angioarchitecture is favourable (scores 0-2). Favourable angioarchitecture includes the pure fistulas and AVMs with a single, dominant, pial, feeding artery.

P-037

Angiographic and Clinical Characteristics in Patients with Cerebral Arteriovenous Malformations Associated with Hereditary Hemorrhagic Telangiectasia

K.G. terBrugge, J.L. Manzia, S. Matsubara, R.A. Willinsky, W. Montanera, M.E. Faughnan (Toronto, Ontario)

Object: Cerebral arteriovenous malformations (AVMs) are occasionally associated with Hereditary Hemorrhagic Telangiectasia (HHT) which is characterized by the presence of multiple mucocutaneous telangiectasia, epistaxis and familial inheritance. We analyzed the angiographic and clinical characteristics in the patients with cerebral AVMs related to HHT.

Methods: Among 638 cerebral AVM patients, we identified 14 patients with HHT. The AVMs were classified into those with a nidus of 1 cm or less (micro AVM), those with a nidus between 1 and 3 cm (small AVM) and those of the fistulous type (AVF)

Results: A total of 28 AVMs were found while 7/14 patients had multiple AVMs. Those 28 AVMs were categorized into 12 micro AVMs, 8 small AVMs, and 8 AVFs. All but one micro AVM were symptomatic, whereas all small AVMs were symptomatic. In AVFs 3/8 were symptomatic. All 28 AVMs were located on the cortex. All micro AVMs and AVFs had a single feeder and a draining vein, whereas small AVMs had multiple feeders in all lesions and single draining veins in 6/8 lesions.

Conclusion: Multiple cortical micro AVMs or AVFs harboring single feeding arteries and single draining veins should raise the clinical suspicion of HHT-related AVMs

P-038

Essential Thrombocytosis as a Cause of Diffuse Cerebral Dysfunction and Multifocal Transient Ischemic Episodes: Case Report and Review of the Literature

C. Toth, A. Rajput, J.R. Donat (Saskatoon, Saskatchewan)

Background: Essential thrombocytosis is a benign condition in most patients, but rarely this can be associated with multifocal central nervous system (CNS) dysfunction.

Methods: We provide a clinical description of a 75-year-old male patient who presented with fluctuating encephalopathy accompanied by transient, discrete episodes of focal CNS dysfunction due to essential thrombocytosis (ET).

Results: A 75-year-old male patient with a prior history of ET acutely developed confusion associated with gait difficulty followed by gradual improvement. Examination one month later revealed diffuse cognitive impairment with focal findings of facial asymmetry, increased tone to right body, impaired cortical sensory function to the left body, and drift of the left arm. After numerous investigations, ventricular shunting was performed for suspicion of normal pressure hydrocephalus, followed by apparent clinical improvement. The patient remained well for three months following before again developing confusion associated with left-sided corticospinal tract findings. The patient returned three days later with increasing confusion and additional left-sided corticospinal tract findings. Again, the patient seemed to improve before returning three days later with marked confusion and numerous focal findings on examination. Intravenous hydration followed by hydroxyurea therapy led to a return to normal functioning. The patient continues to do well three months later on antiplatelet therapy and hydroxyurea.

Conclusion: ET can present as diffuse cerebral dysfunction with focal features.

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P-039

Neurologic Presentations of Intracranial Artery Dolichoectasia: Case Series and Review of the Literature

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Background: Dolichoectasia of intracranial vessels can present with features of ischemia or mass effect and is reported as a cause of stroke uncommonly.

Methods: We describe the clinical and radiologic assessment of eleven patients presenting with neurologic dysfunction associated with identified dolichoectasia on diagnostic imaging.

Results: Eleven patients presented to our institution with neurological dysfunction due to detected dolichoectasia. Eight males and three females, mean age of 60 years (range of 17-75 years), had dolichoectasia identified on computerized tomography or magnetic resonance imaging of the brain or angiography. Neurologic dysfunction consisted of stroke(s) in 7 patients, headache in 2 patients, trigeminal sensory neuropathy in 2 patients, abducens palsy in 1 patient, unilateral sensorineural hearing loss in 1 patient, trigeminal neuralgia in 1 patient, hemifacial spasm in 1 patient, and hydrocephalus in 1 patient. Dolichoectasia was seen in the posterior circulation in all eleven patients and in the anterior circulation in three patients.

Conclusion: Dolichoectasia can produce ischemia via aneurysmal thrombosis, occlusive thrombosis of perforating arteries, or distal embolism, as well as compression of brainstem structures and cranial nerves via mass effect. Dolichoectasia is a rare cause of stroke, but should be considered in patients with concurrent cranial nerve palsies, brainstem compression signs, or hydrocephalus.

P-040

Surgery of Deep and Brainstem Cavernous Malformations at the Toronto Western Hospital

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The incidence of adverse neurological events in patients harboring deep cerebral (thalamic) or brainstem cavernous malformations is 10.6%/yr, prompting a desire to treat these lesions. Of 303 cavernoma patients at the Toronto Vascular Malformation Clinic, 83 have brainstem and 18 have thalamic cavernomas. Of these, 14 brainstem (3 midbrain, 7 pons, 4 medulla) and 1 thalamic cavernoma patients underwent surgery between Jan 1, 1997 and Dec 31, 1999. All patients presented with hemorrhage and/or recurrent adverse neurological events, and were deemed to have surgically accessible lesions. Surgery was performed using skull base techniques including modified trans-petrosal approaches and with intraoperative frameless stereotaxy. Follow-up ranged from 4-34 months.

Results: There were no neurological complications from surgery in the pons and medulla. The patient with a thalamic lesion suffered a transient hemiparesis (recovered). 2 patients with midbrain cavernomas suffered worsening of neurological symptoms (1 ataxia-recovered, 1 hemiparesis, improving). 1 patient with a medullary cavernoma died 3 months post-op from respiratory impairment (present pre-op).

Conclusion: Surgery of deep and brainstem cavernomas is feasible in appropriately selected patients with mortality/ permanent morbidity of under 10%. The degree of pre-operative impairment dictates post-operative neurological status.

P-041

Recurrent Intracerebral Hemorrhage of Unknown Etiology Associated with High Titre of Anticardiolipin Antibody

M.R. Ursell, S.E. Black (Toronto, Ontario)

Background: Anticardiolipin antibody is an established risk factor for ischemic stroke in the young, with a prevalence ranging from 5 to 38% in ischemic stroke populations. The relationship between anticardiolipin antibody and hemorrhagic stroke is unknown. There are 5 reported cases of intracranial hemorrhage associated with high antiphospholipid antibody titres in which no other etiology for the hemorrhage could be found.

Methods: We present a case of recurrent intracerebral hemorrhage of unknown etiology in a man whose only potential stroke risk factor was isolated high titre of anticardiolipin antibody. Serial CTand MRI scans of the brain, angiography and histopathology from biopsy tissue will be presented.

Results: A 55-year-old man presented with severe headache and behavioural changes. A CT scan of the brain revealed bilateral frontal intracerebral hematomas. He was normotensive without identifiable stroke risk factors. Brain biopsy on two occasions was negative for neoplasia, vasculitis and amyloid angiopathy. He presented with recurrent headache eighteen months later and was diagnosed with a new left frontal intracerebral hematoma. Serial MRI scans with and without gadolinium were unhelpful in establishing a diagnosis. Two years later he presented with a generalized seizure associated with a new resolving left temporal hematoma. This was followed two weeks later by progressive loss of consciousness and left hemiparesis. A CTscan showed acute right frontal lobe and right temporal lobe intracerebral hemorrhages. MR venogram and cerebral angiography were negative for thrombosis and structural abnormality. An extensive stroke workup including serology for collagen vascular disease was negative, however anticardiolipin antibody titre was consistently high positive at greater than 100 GPL.

Conclusions: Anticardiolipin antibody may be a risk factor for intracranial hemorrhage. High titres of antiphospholipid antibodies as a potential cause for otherwise unexplained intracerebral hemorrhage should be considered in normotensive patients without other identifiable stroke risk factors.

P-042

Single Stage Surgical Excision of High-Grade Brain Arteriovenous Malformations

M. West (Cleveland, Ohio)

Background: Proposed treatment strategies for high-grade (Spetzler and Martin grade 4 and 5) brain arteriovenous malformations (AVM) have included surgical excision (either

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staged, or not), stereotactic radiation, endovascular embolization and combinations of the above. The present study documents the results of single-staged surgical excision of high-grade AVM, without embolization.

Methods: 22 patients (pt.) were treated; 11 males, 11 females. Age ranged from 15 to 53 years (mean 30.4). 12 AVM were in the dominant hemisphere. 19 pt. (86.4%) had grade 4 lesions. 3 pt. (14.6%) had grade 5 lesions. Clinical presentation was due to a.) intractable seizures – 54.5%, b.) hemorrhage – 27.3%, and c.) progressing neurological deficit – 13.6%. Surgical excision was performed at one operation (surgery time 7-22 hours; mean 13.6 hours) in all cases and complete AVM excision was confirmed by intra-operative cerebral angiography.

Results: There was no surgical mortality. 1 pt. developed a brain abscess, had surgical drainage, and made a full recovery. 1 pt. had transient dysphasia. 3 pt. developed new visual field defects. The presenting neurological status was improved in 5 cases (22.7%), unchanged in 14 cases (63.6%), and worse in 3 cases (13.6%). 18 pt. (81.8%) resumed their normal occupations. 4 pt. (18.2%) were independent but unable to work.

Conclusion: Symptomatic high-grade brain arteriovenous malformations can be removed at a single operation with acceptable morbidity and mortality.

CHILD NEUROLOGY

P-043

Numb Chin Syndrome in a Fourteen-year-old Female

G. Blevins, E. Wirrell, N. Lowry (Saskatoon, Saskatchewan)

Introduction: Numb chin syndrome, or mental neuropathy, is well described in adults. The diagnostic implications have also been clearly reported. To our knowledge, there has not previously been a description of this presentation in the pediatric age group.

Case Report: A14 year-old female presented with a three-week course of anaesthesia, initially unilateral and becoming bilateral within one day, in the distribution of the mental nerves. Additionally, the patient began to complain of neuralgic pain in the distribution of the inferior alveolar nerves. It was noteworthy that other than these complaints, there were no further neurological or constitutional features. On examination, the only finding was anaesthesia restricted to the distribution of the mental nerves. A tomogram demonstrated lytic lesions within the mandible with interval change from a mandibular tomogram performed 2 weeks prior at another institution. Acore biopsy obtained from this region established the diagnosis of Burkitt's lymphoma. The patient received further medical imaging, which demonstrated disease involving paravertebral lymph nodes, breasts, kidneys and ovaries. Involvement of these locations was asymptomatic.

Conclusion: We demonstrate a pediatric patient with numb chin syndrome. This case, as previously described in the adult population, presented only with this complaint, which on the outset appears very benign. Numb chin syndrome has a nearly invariable association with malignancy involving the course of the inferior alveolar nerve. As demonstrated in this case, recognition of the numb chin syndrome in pediatric patients has the same connotations as in adult cases.

P-044

Acute Disseminated Encephalomyelitis: A Re-emerging Entity

C. Campbell, D. Keene, H. Dunlap, P. Humphreys (Ottawa, Ontario)

Background: Acute disseminated encephalomyelitis (ADEM) or post viral encephalitis is an uncommon virally triggered demyelinating condition seen primarily in children. ADEM has its clinical origins in reports following measles infection from the early part of the twentieth century and is represented experimentally by experimental allergic encephalitis. Recent descriptions of clinical, radiographic and laboratory features have made this condition more easily distinguished from true viral encephalitis and other para-infectious encephalopathies. As yet no definitive set of diagnostic criteria exist and treatment remains based on anecdotal evidence.

Methods: Clinical reports of two children diagnosed and managed at the authors'centre and a review of the literature.

Results: Both children experienced a monophasic illness following a viral infection that was characterized by fever, headache and altered behaviour and level of consciousness. Cerebral spinal fluid demonstrated mild pleocytosis and elevated protein in both children and magnetic resonance imaging findings consistent with bilateral, primarily subcortical, demyelinating lesions. Both patients eventually returned to normal functioning, but one patient was treated with intravenous gama globulin (IVIG) based on several case reports and has had an excellent response returning to normal by three months.

Conclusions: The uncommon nature of ADEM has clearly impacted on the timely recognition of this condition and the ability to study therapeutic interventions. Diagnostic characteristics of the illness are suggested as are strategies for raising national awareness. In one of our cases IVIG improved the clinical condition quickly without obvious adverse affects.

P-045

Medical and Cognitive Outcome of Moderate and Severe Head Injury in Children

C. Campbell, P. Richards, E. Ventureyra, S. Kuehn, J. Hutchison (Ottawa, Ontario)

Background: Head injury is an important cause of morbidity and mortality in pediatrics. Comprehensive studies on the outcome of children with head injury are scarce despite significant clinical concern that multiple areas of functioning may be impaired following head injury. The complications include not only medical problems, but also impairment of intelligence and memory.

Methods: Retrospective medical and psychological chart review of patients admitted to the Children's Hospital of Eastern Ontario with moderate and severe head injury (Glasgow Coma Scale ≤12) in the years 1994-1997.

Results: Forty-six children, aged five to seventeen, with moderate and severe head injury were reviewed. Multiple medical complications were documented such as seizures and headaches. The mean verbal and performance intelligence

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quotient (IQ) was below normal at the baseline assessment (1-2 months post injury), but improved into the normal range by 6-12 months. The variability was large. The mean memory score was also below normal at baseline assessment. Although a trend to improvement over time was seen, at 18-24 months the mean memory scores remained below the normal range. Again variability was large.

Conclusions: Multiple medical complications and significant cognitive dysfunction is noted following head injury. Mean verbal and performance IQ improve over time into the normal range but great variability was seen. Persistent impairments in memory were seen two years post injury.

P-046

Salmonella Intracranial Abscess and Hydrocephalus in a Newborn.

S.D. Christie (Halifax, Nova Scotia), S. Walling (St John, New Brunswick).

Background: Focal intracranial abscesses are uncommon complications related to infections of Salmonella species. A review of the world literature from 1884 until present revealed only 33 cases. Only 5 were from the neonatal period. Commonly associated complications include: seizures, hydrocephalus, subdural empyemas and ventriculitis. Mortality for intracranial salmonella infections approaches 20%. Herein we report the first case of salmonella cerebral abscess reported in Canada.

Methods: A review of the literature and report of clinical case.

Results: A 4-day-old boy presented with meningitis following an uncomplicated pregnancy. CTscan revealed evidence of a left parietal abscess and hydrocephalus. Management included antibiotics, surgical drainage and CSF diversion. Cultures grew Salmonella serotype agona. Retrospective review revealed an episode of maternal enteritis at 6 months during the pregnancy. Subsequent cultures from the mother were consistent with conversion to carrier status. The child is slow to obtain neurologic milestones and has been plagued with multiple shunt dysfunctions.

Conclusions: Focal intracranial complications of salmonella infections are rare but can lead to devastating neurologic complications despite prompt and appropriate management.

P-047

Intrauterine Loss of Leg Function in Children with Spinal Dysraphism

R.F. Del Maestro (London, Ontario)

Background: Prenatal screening and obstetrical ultrasound identifies the majority of fetuses with spinal dysraphism. In our centre, these fetuses are followed prospectively with obstetrical ultrasound to monitor a number of growth parameters. During these studies two have been identified who initially had normal leg function and morphology and lost leg function in utero. This presentation discusses their assessment and management.

Methods: Prospective studies of obstetrical fetal ultrasounds were carried out in all children with spinal dysraphic states. The parameters studied were 1) the development of hydrocephalus; 2) changes in myelomeningocoele size; 3) leg function and morphology.

Results: At 19 weeks gestational age the first fetus had normal leg function and morphology. At 24 weeks right leg function appeared normal while left leg function was less brisk. At 28 weeks no movement of the lower extremities was observed and the left foot remained flexed and inverted suggesting a clubfoot deformity. No leg function was observed on subsequent ultrasounds and the child was delivered by caesarean section at 37 weeks gestational age. The child had a complete spinal myelopathy with lower extremity contractures, a fixed subluxation of the right hip and hydrocephalus. The neural placode appeared to have been destroyed and only a vascularized membrane remained. The second child was initially seen at 18 weeks gestational age and had normal leg function. On subsequent ultrasound the leg movement remained normal. At 36 weeks the mother noted a sudden decrease in fetal movement. Emergency obstetrical ultrasound demonstrated no leg movement. The child was delivered by caesarean section. Some hip, knee and ankle movement was seen and an incomplete spinal myelopathy was present. At two years of age the child has L3 and some L4 function.

Conclusions: Sudden loss of leg function may occur during intrauterine development in some fetuses with spinal dysraphism. This may be due to intrauterine destructive process involving the neural placode. Periodic obstetrical ultrasounds should be carried out to monitor leg function and emergency caesarean section may be crucial to try to salvage leg function.

P-048

X Linked Hydrocephalus and Hirschsprung's Disease

R.F. Del Maestro (London, Ontario)

Background: The occurrence of X linked hydrocephalus and Hirschsprung's disease in two male siblings in a family in which the mother is known to be a carrier highlighted the possible genetic relationship of these two disorders. X linked hydrocephalus is associated with congenital stenosis of the aqueduct of Sylvius and is characterized by mental retardation, spastic tetraparesis and hand abnormalities (bilateral adducted thumbs). Genetic abnormalities in the LICAM gene, a member of the immunoglobin gene superfamily of the neural cell adhesion molecules underlie this syndrome. Hirschsprung's disease is a neurocristopathy with characteristic absence of parasympathetic ganglion cells in the lower bowel. A Japanese child with X linked hydrocephalus and Hirschsprung's disease has been found to have a 2 base pair deletion of exon 18 of the LICAM gene (Okamoto et al, J. Med Genet. 34, 670-671, 1997).

Methods: Family tree analysis identified the presence of X linked hydrocephalus in three generations with two affected males succumbing at birth and early infancy. Only the two siblings reported here have been diagnosed with Hirschsprung's disease. Both have undergone ventriculoperitoneal shunting and one child was treated with a colostomy in the neonatal period and later abdominal-perineal pull through procedure. The second awaits the pull through procedure. Female carriers have been identified by linkage studies in this pedigree.

Conclusions: Since LICAM is one component of an interactive network of cell adhesion molecules, signaling

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components and cytoskeletal arrays it is not surprising that genetic abnormalities in this molecule give rise to both X linked hydrocephalus and a disorder of migration of the neural crest cells, Hirschsprung's disease.

P-049

Parent Perceptions of the Value of Pediatric Neurology Clinic Visits

J Dooley, K Gordon, E Wood (Halifax, Nova Scotia)

Rationale: To evaluate families' perceptions about the value of pediatric neurology clinic visits and alternate methods of delivering care.

Methods: 200 consecutive families were given 2 questionnaires on arrival at the clinic. The first questionnaire was completed before the visit and the second after. The first asked why the child was in clinic and whether it was a new referral, routine follow-up or because of new concerns. They detailed demographic data, time missed from school or work and impact of travelling, including cost. In both questionnaires they were asked if the visit could have been by telephone, videoconference or with a nurse. The second questionnaire rated multiple aspects of the value of the visit and asked if follow-up was necessary, and if so with whom and how.

Results: There were 172 (86%) responders: 58 new referrals, 73 routine follow-ups and 37 because of new concerns. Demographic features will be presented. The appointment was considered necessary by all but 4 (2%), who were more likely to consider telephone as an appropriate assessment modality ($p<0.001$). Initially only 14/168 thought the visit could have been by telephone and 15/165 (9.1%) by videoconference. The mean distance traveled was 109 Km, but some traveled >1000 Km each way. Cost was a concern for 11 (6.4%) and was not related to lost pay which was reported by 33 (19%). The mean reported expense was $29.98. After the visit 103/107 (96%) thought the visit was helpful. The visit overall was rated as very good or excellent by 119/134 (89%). In retrospect 24% considered an alternative to routine care acceptable – 16/132 (12%) thought the visit could have been with a nurse, 13/134 (10%) by telephone and 12/134 (9%) by videoconference. Follow-up was considered necessary by 58/129 (45%), with the pediatric neurologist for 94% and in person for 90%.

Conclusions: Families are satisfied with current care delivery and are reticent to accept replacement by a nurse or by either telephone or videoconference. These opinions must be respected with planning innovations to methods of following patients.

P-050

Spinal Cord Involvement in a Male Child with Systemic Lupus Erythematosis

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Background: Spinal cord involvement is a rare and serious manifestation of systemic lupus erythematosis (SLE). There are 12 pediatric reports of transverse myelitis. All are female. The cervical and thoracic cords are most commonly affected. The only previous report of conus medullaris involvement is a 32-year-old female.

Case Report: Two months after diagnosis of SLE a previously healthy and neurologically normal 14-year-old male presented with urinary symptoms, constipation and leg weakness. Neurologic examination revealed cognitive difficulties. Weakness of plantar flexion and dorsiflexion was present. Lower limb deep tendon reflexes were brisk and plantar responses were extensor. The left lower quadrant abdominal and left cremasteric reflexes were absent. Vibration and position sense was diminished. T2 weighted MRI showed increased signal intensity of the conus medullaris and bilateral cerebral white and grey matter. He was treated with methylprednisolone and cyclophosphamide. An initial response was documented, however he rapidly progressed.

Conclusion: This is the first reported male with SLE and spinal cord disease, and the first pediatric case of lumbar and conus involvement. In spite of aggressive early therapy, it may be refractory to combined methylprednisolone and cyclophosphamide.

P-051

Hemiparetic Cerebral Palsy: Clinical Pattern and Imaging in Prediction of Outcome

Peter Humphreys, Sharon Whiting, Ba'Pham (Ottawa, Ontario)

Background: Hemiparetic cerebral palsy (HCP) is described as having two main forms: arm-dominant, associated with large cortical/subcortical lesions; leg-dominant, associated with lesions of central white matter. Epilepsy and cognitive deficits are common in the former pattern and rare in the latter. Some authors have recommended routine imaging studies in children with HCP as an assessment of etiology and a predictor of outcome. The present study compares the relative values of clinical analysis and imaging in predicting epilepsy and cognitive disabilities.

Methods: 41 consecutive patients with HCP underwent careful clinical assessment and imaging studies (primarily computed tomography) and were followed prospectively for the development of recurrent afebrile seizures and academic difficulties.

Results: 20/41 patients (48.8%) were arm-dominant, 14/41 (34.1%) leg-dominant, and 7/41 (17.1%) proportional (arm = leg). The principal imaging findings were: arm-dominant patients - large arterial infarcts, porencephalic cysts, brain malformations; leg-dominant - periventricular leukomalacia; proportional - porencephaly. Arm-dominant hemiparesis and radiologic evidence of cortical pathology were both predictive of cognitive deficits (odds ratios 14.2 [95% CI 2.6, 75.8] and 5.7 [95% CI 1.4, 22.3] respectively). For the development of epilepsy, both evaluation techniques were again predictive, with imaging findings of cortical pathology being particularly powerful (clinical pattern OR 18.0 [95% CI 3.0, 107.7]; imaging OR 80.7 [95% CI 8.5, 767.3]).

Conclusions: In this study, the clinical pattern of HCPand the radiological findings were both predictive of outcome, with absence of cortical pathology on imaging being particularly

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predictive for the absence of epilepsy. While the clinical pattern, in isolation, appears helpful in predicting outcome, our results suggest that both evaluation tools have important roles to play in the evaluation of HCP patients.

P-052

Cerebral Vascular Disease in Association with Acute Inflammatory Bowel Disease in Children

D. Keene, P.Jacob, and P. Humphreys (Ottawa, Ontario)

Rationale: Inflammatory bowel disease can have many complications outside the gut. Among these peripheral vascular thromboembolic events have been recognized as a serious extra-intestinal complication. Cerebrovascular diseases have been rarely reported.

Method: A series of cases of cerebrovascular events in children at the time of an acute exacerbation of their underlying inflammatory bowel disease are reported.

Results: 3 children ages 5, 12 and 13 years presented with clinical and MRI evidence of an acute cerebrovascular event in association with an acute exacerbation of their inflammatory bowel disease. Steroids failed to control the bowel disease. Degree of acute rectal disease in each case was sufficient to warrant acute surgical intervention. Except for anemia, no abnormalities were noted in any of the patient's hematological profile or coagulation studies. Search for evidence of a systemic vasculitis proved negative. Reoccurrences did not occur after the bowel disease was under control.

Discussion: A med-line search found a further 10 cases of CVAassociated with inflammatory disease in children. Mean age of presentation was 14 years (range 12 to 18 years). Sex distribution was equal. Thrombotic events occurred in the arterial territory occurred in 5 cases. The duration of the inflammatory bowel disease prior to thrombotic event was shorter in patients with venous sinus thrombosis than arterial (2 months compared to 24 months). Consistent changes in hematological and coagulation studies at the time of the event were not noted. Nor was evidence of systemic vasculitis was found.

Conclusion: Cerebral vascular events can be a rare complication of inflammatory bowel disease in children. The etiology of this association remains unknown.

P-053

Progressive Intellectual and Neurological Deterioration in Pediatric Population (PIND)

D. Keene, T. Suttcliffe and Canadian Pediatric Surveillance Program (Ottawa, Ontario)

Objective: Creutzfelt-Jacob Disease (CJD) and new variant CJD are rare cases of neurological deterioration in childhood. In order to assess if complete ascertainment of these disorders has occurred, an enhanced active surveillance system for progressive intellectual and neurological diseases was implemented in Canada to prospectively detect all persons presenting to their attending physician with this problem.

Case Definition: Inclusion criteria was all persons under the age of 18 years with a 3 month history of progressive deterioration of already attained intellectual abilities and the development of abnormal neurological signs. This included metabolic disorders, seizures with progressive deterioration in development abilities, and disorders with specific neurodegenerative diagnosis. Static encephalopathies were excluded.

Cases Ascertainment: The participating physicians in the Canadian Pediatric Surveillance System (included pediatricians, family doctors, and pediatric neurologists) each month were requested to send a standardized report card to complete. More detailed data was requested on identified cases. A panel of pediatric neurologists reviewed and classified the ascertained cases according to diagnosis.

Results: The surveillance began in July, 1999. In the first 5 months, 24 cases have been reported. 11 have had sufficient data to classify; on the rest more detailed case descriptions have been requested. Of the classified cases included the following diagnosis: mitochondrial disorders 5; muccopolysaccaridosis 3, Rett's 1; adrenoleukodystrophy 1: CJD 1. The case of CJD was reported by 5 different reporting physicians.

Conclusion: National surveillance of complex rare neurological disorders can be done using a network of dedicated physicians.

P-054

An Examination of Intelligence and Memory Functioning in Children Treated for Posterior Fossa Tumors

A. George, S. Kuehn, A. Modha, M. Vassilyadi, E. Ventureyra, P. Richards, S. Parlow (Ottawa, Ontario).

Background: Late effects of radiotherapy on intellectual functioning have been well documented in children treated for posterior fossa tumours. Other aspects of cognitive functioning, such as memory, have not been adequately examined in this population. This retrospective study reports on 15 children treated for medulloblastoma (N=11) and cerebellar astrocytoma (N=4).

Methods: Children were administered norm-referenced, standardized tests of intelligence (i.e., Wechsler Scales) and memory functioning (i.e., Wide Range Assessment of Memory and Learning). The assessments were conducted an average of 3.5 years after radiotherapy.

Results: Analyses revealed sample means for IQ and memory were significantly lower than those of the normative population. No significant differences were found between the Verbal and Performance IQ, or Verbal and Visual memory. A stepwise regression analysis revealed that age at diagnosis accounted for a significant proportion of variance in the intelligence ratings. The IQ scores of children less than 6 years of age at diagnosis were significantly lower than those of children diagnosed over the age of 6. Neither age at diagnosis nor time since treatment accounted for a significant proportion of the variance in the memory indexes.

Conclusions: Follow-up assessments of memory functioning conducted more than five years post-treatment may better identify the long-term effects of radiotherapy.

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P-055

Long Term Outcome of Infants Following Perinatal Acute Total Hypoxic Ischemic Encephalopathy (ATHIE)

S.D. Levin, C.P. Iliffe, A.M. Fox, (London, Ontario)

Background: The experimental model of acute total hypoxic-ischemic encephalopathy (ATHIE) demonstrated by Myers in 1972 showed selective damage to the brainstem, basal ganglia and thalamus and relative sparing of the cerebral cortex. This paper documents the long term clinical outcome of children who survive ATHIE.

Method: From a retrospective survey of 120 patients with perinatal HIE, seven were found to fulfill our criteria for ATHIE. Three of these infants survived. We report on these 3 children who have now been followed up to 3-5 years of age.

Results: All infants sustained a significant hypoxic ischemic insult resulting in encephalopathy defined by Apgars < 5 at 5 minutes, arterial cord pH of ≤7.2 and significant encephalopathy persisting beyond 24 hours of life. Imaging studies demonstrated isolated injury to basal ganglia, with relative sparing of the cortex. Long term follow up at 3, 4 and 5 years demonstrated truncal hypotonia, bilateral dystonic hemiparesis and choreoathetosis. Cognitive function has been relatively preserved compared to motor abilities. Two of the three infants are now felt to be socially and cognitively normal, the third has mild developmental delay but is doing relatively well compared to her motor progress. Head circumference is within normal range in two of these infants and below the 3rd percentile in one. All have evidence of facial weakness, feeding difficulties and dysarthria consistent with brainstem injury. Two have seizures but do not require treatment with anti-epileptic drugs. Fine motor function has been relatively preserved but there is limited gross motor function in all three. One child can walk independently, one walks with assistance and the other requires a wheelchair.

Conclusion: Acute total hypoxic ischemic encephalopathy (ATHIE) has a different long term outcome from most cases of prolonged partial hypoxic ischemic encephalopathy. We should anticipate these differences to provide appropriate therapeutic support.

P-056

Molecular DNAAnalysis and Biochemical Characterisation of the Neuronal Ceroid Lipofuscinoses

S. D. Levin, J. Rip, C.A. Rupar (London, Ontario)

Background: The neuronal ceroid lipofuscinoses (NCLs) are a group of neurodegenerative disorders characterised clinically by progressive myoclonic epilepsy, cognitive decline, ataxia and visual loss and ultrastructurally by the accumulation of autofluorescing lipopigment in lysosomes. At least 8 genes (CLN1-8) underlie the NCLs of which four have been isolated and mutations characterised: CLN1, CLN2, CLN3 and CLN5. Two of these genes encode lysosomal enzymes and two encode transmembrane proteins, at least one of which is likely to be in the lysosomal membrane.

The development of molecular DNA analysis for these diseases and sensitive protease activity assay characterising the CLN2 gene product abnormal in late infantile NCL cases mutations allows precise diagnosis of patients and prenatal diagnosis by chorionic villus sampling.

Methods and Results: To date tripeptidyl peptidase I assays have been performed on 7 clinically well characterised patients with late infantile NCL. 6/7 patients demonstrated deficiency of this enzyme. Mutation analysis has been completed on 4 patients and 8 mutations identified. 6/8 mutations were identified as either a G to C mutation at nt 3556 or a C to T mutation at nt 3670.

Two patients with juvenile NCLrevealed 4 mutations, all 1.02 kb deletions in the CLN3 gene.

Conclusions: Recent advances in molecular and biochemical disorders now allow for precise diagnosis in patients and antenatal diagnosis. Biochemical characterisation of the gene products can also be used for diagnosis and has revealed a group of metabolic abnormalities not previously known to cause disease.

P-057

Craniocervical Arterial Dissection in a Paediatric Population

Daune MacGregor (Toronto, Ontario) and the Canadian Pediatric Ischemic Stroke Study Group: C. Adams, M. Adams, M. Andrew, F. Booth, B. Bjornson, D. Buckley, C. Camfield, A. Chan, S. Christie, R. Curtis, M. David, G. D'Anjou, G. deVeber, P. Flavin, G. Geoffroy, J. Gillett, P. Humphreys, D. Keene, S. Lanthier, Ms. S.E. Lee, E.A. MacDonald, D. MacGregor, S. Mayank, D. Meek, P. McCusker, B. Prieur, M. Shevell, B. Sinclair, J. Tibbles, E. Wood, J. Wu, J.Y. Yager.

Background: Arterial dissection in children is infrequently reported. The contribution of dissection to childhood arterial ischemic stroke (AIS) has not been established.

Method: Within the Canadian Paediatric Ischemic Stroke Registry database of arterial ischemic strokes, (n=660), 27 children diagnosed with cranio-cervical arterial dissection have been identified from January 1992 to January 1998 at 16 paediatric tertiary centres. All 27 cases were interpreted by local radiologists or clinical reports as having "dissection".

Results: Of arterial ischemic strokes, 27 (4%) patients (15 males, 12 females) with acute dissection were identified (9 vertebral, 14 internal carotid, 4 unspecified) ranging in age from 3 months to 16 years (median 13.2 yrs.). Clinical presentations were: headaches (52%) and other signs of intracranial pressure (70%), hemiparesis and cranial nerve abnormalities (30%), hemiplegia (19%), dysarthria (19%), aphasia and ataxia (14% respectively). Head or neck trauma was a predisposing factor in 12 (44%) patients. The initial diagnosis of AIS was made by CT scans in 78% and MRI in 22% of the cases. Infarcts were single in 33% and multiple in 59% and there were 2 with intracranial hemorrhage. Conventional angiography was completed in 23 (85%) patients, with MRA in 9 (33%) patients. Antithrombotic treatment was given in 21 patients and included: standard heparin 71%, low molecular weight heparin 38%, coumadin 76%, and/or aspirin 38%. Of 16 patients for whom there was

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complete follow-up data, 75% had mild to moderate neurological deficits. Further cerebral infarcts or TIAs occurred in 6 (22%) patients. Mortality was 11%.

Conclusions: Arterial dissection is likely underestimated, and is only diagnosed in 4% of childhood AIS. Non-standardized radiographic criteria probably result in underdiagnosis. Almost 50% are post-traumatic. More than 75% are treated with antithrombotic agents and AIS recurrence rate is 22%. Given the risk of recurrence, clinical definition and treatment need to be studied.

P-058

Delving into the Brain-Behavior-Genetics Connection; What Can Neurologists Learn from Genetic Disorders?

A. Prasad, C. Prasad, B. Chodirker, A. Chudley (Winnipeg, Manitoba)

Background: In the last decade, unique neurobehavioral phenotypes have been recognized amongst genetic syndromes. The recognition of behavioral phenotypes serves as a basis to link cognitive deficits, brain abnormalities and their genetic underpinnings.

Methods: A literature review of characteristic behavioral phenotypes within commonly diagnosed genetic syndromes was undertaken. Next, an estimate of the relative frequencies with which these genetic syndromes are encountered in a referral clinic setting was obtained through a computerized search of the clinic database.

Results: Reflecting the literature, the following numbers of diagnoses made through the genetics clinic provide an estimate of the frequency with which these genetic syndromes are encountered. Fragile X (63), Prader-Willi syndrome (39), Rett syndrome (21), 22q11 deletion syndrome (11), Angelman syndrome (8), Williams syndrome; Smith Magenis (4), and the 22q11.3 terminal deletion syndrome (2). Using illustrative case reports for each of the above syndromes, data on the relevant genetic dysmorphic features, specific neurobehavioral phenotype, neuropathological and neuroimaging findings and molecular genetic correlations is presented.

Conclusions: Genetic dysmorphic syndromes offer a unique insight into the inter-relationship of brain-genes-behavior. To neurologists, the ability to recognize specific behavioral phenotypes offers an opportunity to improve on diagnosis and management of these conditions, and learn more about gene regulation of behavior.

P-059

Acute MotorAxonal Neuropathy in Children

V. Vedanarayanan, H. Bell, O.B. Evans and S.H. Subramony (Jackson, Mississippi)

Background: Acute motor axonal neuropathy (AMAN) is an acquired progressive generalized areflexic motor weakness and is characterized by predominantly motor axon injury. Griffin and colleagues have described pathological features of this condition and helped establish its etiological relationship with *Campylo - bacter jejuni* infection on studies in Chinese children.

Objectives: To describe the clinical features and electrophysiological data in two children with AMAN associated with *Campylobacter jejuni* infection.

Clinical Data: WAM, a 15-year-old boy presented with one week history of progressive symmetric weakness of distal lower limb muscles after suffering from watery diarrhea a week prior to that. He had no sensory loss and had areflexia distally. The CSF examination was normal, serological studies for glycolipids antibodies, antibodies to polio and enteroviruses, ANA and rheumatoid factor were normal. Antibodies to *Campylobacter jejuni* was increased. The electrodiagnostic studies showed reduction in motor CMAP with evidence of denervation of leg muscles on electromyographic examination. The strength improved gradually over the next 6 weeks and repeat electrodiagnostic studies showed improvement of motor CMAP.

JLW, six-year-old boy presented with 3 day history of progressive symmetric lower limb weakness with no pain or sensory symptoms. There was no sensory loss with areflexia in distal lower limb muscles. The CSF protein was increased with normal cell count. The antibodies to *Campylobacter jejuni* were increased. He was treated with intravenous immunoglobulin with gradual improvement in strength. The electrodiagnostic studies showed reduction in motor CMAP with normal sensory responses. Repeated studies showed progressive decline in motor CMAP with evidence of denervation. With clinic improvement in distal CMAP was seen.

Conclusion: We have reported two children with AMAN associated with *Campylobacter jejuni* infection. The electrodiagnostic studies are helpful in recognizing this condition.

DEMENTIA

P-060

Oculoleptomeningeal Amyloidosis: An Autosomal Dominant Form of Dementia

G. Blevins, S. Harder, J.R. Donat (Saskatoon, Saskatchewan)

Introduction: Familial amyloidosis is a group of autosomal dominantly inherited diseases, which result in the deposition of amyloid protein in target tissues. Recently several families have been described with predominant involvement of the eyes and meninges. This form of amyloidosis, termed oculolepto-meningeal amyloidosis, has been associated with mutations in the transthyretin gene.

Case Report: A 48-year-old male presented to our institution with a history of recurrent multifocal symptoms. Six years previously, he had had an episode of transient left hemiparesis. Two years later, he had transient right hemiparesis with aphasia and a generalized seizure. One year later, he had two episodes of transient right hemiparesis. Six months prior to presentation, he had three episodes of generalized tonic-clonic seizures. Cerebrospinal fluid (CSF) showed elevated protein. Magnetic resonance imaging showed diffuse leptomeningeal thickening and enhancement. Gingival and skin biopsy demonstrated amyloid deposition. An older sister died after a chronic illness with seizures and progressive dementia. Similarly, the patient's

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father died with the same symptoms and his autopsy revealed meningeal amyloidosis.

Conclusion: We report a family with an autosomal dominant form of dementia as the result of oculoleptomeningeal amyloidosis. Results of sequencing the proband's transthyretin gene is pending.

P-061

Clock Drawing and Longitudinal Assessment in Alzheimer's Disease

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

Clock drawing is a brief and easy-to-administer measure of cognition in Alzheimer's disease (AD). We compared clock drawing and the Mini-Mental State Examination (MMSE) for detecting progression in AD.

We reviewed charts of all patients from the Behavioural Neurology Clinic at Baycrest Hospital with probable AD. Patients studied (n=42) had clock drawing and a MMSE at baseline and follow-up (mean 25.8 months), MMSE score > 10, and were on donepezil. There were three clock conditions with time setting at 10 after 11: free drawn, pre-drawn (circle without numbers), examiner (pre-drawn circle with numbers). Clocks were scored according to published criteria (Freedman et al., 1994). Differences in follow-up and baseline scores were analysed using a paired student t-test.

Patients were separated according to baseline MMSE, Group 1 (MMSE=11-19/30, n=19), Group 2 (MMSE≥ 20, n=23), and had comparable age, education and duration of follow-up. In group 1, the free drawn clock score declined by 9.5 percentage points (p=0.02) while the MMSE remained stable. In group 2 there was a trend towards a decline in MMSE score.

In conclusion, free drawn clocks show more rapid deterioration than MMSE scores in moderate AD, and are useful for longitudinal assessment in this group.

P-062

Serum Methylcitric Acid Levels Correlate with Cognitive Scores in Non-Demented Elderly Subjects

A. Garcia, L. Evans (Kingston, Ontario), M. Freedman (Toronto, Ontario).

Background: The metabolite Methylcitric Acid (MCT) is an early marker of Vitamin B12 (B12) deficiency at the cellular level. Metabolite determinations have been proposed as better markers of B12 function than levels of B12 levels themselves. Both B12 deficiency and dementia are very common among the elderly population. It is unclear if longstanding B12 deficiency causes or contributes to dementia.

Methods: Community volunteers, age 65 and over with Mini Mental Score Exam >23 and no history compatible with dementia, were eligible for testing. The following were also exclusion criteria: strokes, head trauma, acute illness, Parkinson's disease or Parkinsonism, depression or psychiatric disease, hypothyroidism and renal failure. Each volunteer completed: the California Verbal Learning Test (CVLT), Mattis Dementia Rating Scale (DRS) and Stroop psychometric tests. Serum for B12 and MCT determinations was obtained at the same time. Data was analyzed by Pearson correlation.

Results: Significant (p< .05-.0005) inverse correlations were found between the MCT levels and the following psychometric scores: DRS Total, DRS Conceptualization, CVLT recall list A 1-5, recall trial 1 and 5, CVLT short delay recall and cued recall, CVLT long delay cued recall, CVLT semantic cluster learning, CVLT discriminability, and false recognition, and contrast B to A. No correlations were found between MCT and the Stroop scores, or between B12 levels and any of the psychometric tests.

Conclusions: Serum levels of MCT, a metabolite that accumulates in B12 deficiency, showed a significant inverse correlation with cognitive parameters of verbal learning, in healthy elderly volunteers. Since verbal learning abnormalities are good predictors of cognitive deficits, our results might suggests that subjects with early deficits of B12 are at risk of developing dementia.

P-063

Idiopathic Normal Pressure Hydrocephalus: a Systematic Review of Diagnosis and Outcome

A.O. Hebb (Halifax, Nova Scotia), M.D. Cusimano (Toronto, Ontario)

Background: Idiopathic normal pressure hydrocephalus (INPH) presents with gait disturbance (GD), dementia and urinary incontinence, with no cause identified. INPH presents later in life and is less responsive to shunting than secondary NPH, and is mimicked by other neurodegenerative disorders. Patient selection for CSF diversion is difficult as no clinical or diagnostic findings reliably predict outcome. The literature was reviewed to identify diagnostic criteria supported by clinical series of INPH patients, and to formulate reasonable prognostic expectations for patients undergoing shunt placement.

Methods: MEDLINE was searched using a defined search strategy and 511 articles were retrieved, 43 of which were included in this review after elimination based on pre-determined criteria.

Results: Clinical series were frequently retrospective, had small patient numbers, and had short or variable follow-up periods with unstandardized evaluation of outcome. Clinical findings suggestive of shunt responsiveness were the complete triad with early GD. Degree of hydrocephalus did not correlate with clinical improvement. Reduction of the subcortical low blood flow area was correlated with improvement in three separate studies with a combined total of 28 patients. Clinical response to prolonged CSF drainage predicted shunt outcome correctly in all cases in two series with a combined total of 24 patients. Overall, 59% of patients improved following shunting and 29% of patients experienced considerable or prolonged improvement. Thirty-one percent of patients had shunt complications and 16% of patients required additional surgery or acquired permanent neurological deficit from the shunt procedure.

Conclusions: Shunting INPH is associated with an approximately 29% rate of significant improvement, and 16% significant complication rate. Enlargement of the subcortical low flow area and clinical improvement secondary to prolonged

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lumbar drainage may provide additive predictive value above clinical and CTcriteria. INPH is likely a conglomerate of various degenerative disorders, and it remains difficult to identify shunt-responsive patients. Future directions of research should focus on the value of ancillary tests, defining the clinical course of a patient with a VP shunt, and the cost effectiveness of shunting INPH. A multi-centre randomized controlled clinical trial which implements defined entrance requirements and functional grading systems to quantify improvement is needed to better describe outcome from shunting in INPH.

P-064

Outcomes of Dementia Treatment Using Patient-Centred, Domain-Specific Visual Analogue Scales

C. Wentzel (Halifax, Nova Scotia), S. Black (Toronto, Ontario), H. Feldman (Vancouver, British Columbia), K. Rockwood (Halifax, Nova Scotia) for the Canadian Open Label Propentofylline Evaluation Study Investigators

Background: An ongoing challenge in the measurement of disease progression in dementia is the clinical meaningfulness of the measures, which have been criticized as not relevant to individual patient problems. We report the outcomes of novel, patient-centred, domain-specific visual analogue scales.

Methods: Patients (n=461) were recruited from 76 Canadian centres to participate in propentofylline drug trials. At baseline, patients and caregivers specified concerns within the domains of cognition, behaviour, function, and leisure activities. Symptom severity was recorded by the physician using a 10 cm visual analogue scale for each domain, with endpoints '0' (normal intellectual function) and '10'(terminal dementia). Additionally, patients and caregivers described their greatest hopes and fears relative to the current symptoms, defining an upper (hopes) and lower (fears) anchor for each scale. Patients were followed quarterly for one year.

Results: Analysis of the individualized outcome measures on a preliminary sample (n=12) did not increase in severity between the baseline assessment and the 12-month follow-up. Symptom severity at 12 months was greater than hoped ($p < .05$), yet less severe than feared ($p < .05$) at baseline, in each of the four domains.

Conclusions: These scales allow patients and caregivers to define clinical meaningfulness, *a priori*. As such, they may usefully enhance standard neuropsychometric testing.

EPILEPSY

P-065

Motor Seizures Ipsilateral to Epileptogenic Lesion

W. Blume, J. Girvin, D. Jones (London, Ontario)

This 16-year-old, right handed, otherwise neurologically intact student began to have medically refractory seizures at age 6 years consisting of left facial twitching, speech arrest, hypersalivation and hyperventilation. Two tonic-clonic seizures preceded by leftward head deviation and one episode of leftward head deviation without secondary generalised seizures had occurred. A slight decrease in the right nasal labial fold was the only neurological abnormality. No abnormality occurred on scalp EEG. CTand MRI revealed a focal high signal abnormality in the left mid frontal gyrus just superior to the frontal operculum.

Subdural recordings revealed left face and left ocular clonic seizures with apparent right inferior Rolandic origin in three occasions and left inferior Rolandic on one occasion. Left Rolandic stimulation elicited a right inferior Rolandic (homologous) seizure with left face then bilateral facial twitching. Interictal spikes appeared abundantly in both Rolandic regions.

Cortical dysplasia was found on the resected left inferior Rolandic corticectomy involving both the inferior pre- and post central gyri avoiding Broca's and Wernicke's areas as well as the arcuate fibres. The patient has been seizure-free for four months on monotherapy.

P-066

Subdural Electrode Localisation by CT and MR Superimposition

F. Bihari, E. Madevu, W. Blume (London, Ontario)

Subdural electrodes are traditionally localised by stereo-skull x-rays with drawings transferred to a generic brain map. Since this method utilises a brain map that does not precisely conform to individual gyral patterns, the precision of localisation is often compromised. Our method of superimposing post-insertion CT images of segmented electrodes and pre-insertion 3D reconstructed MR images of segmented brain, overcomes these localisation limitations.

Full head, stacked T2 MR images were acquired with Zip to 1 mm protocol on a GE Signa 1.5T scanner prior to insertion of subdural electrodes. The 256x256 images were imported into 3Dviewnix (University of Pennsylvania) running on a Linux workstation. Three-dimensional reconstruction was performed on the data with brain and skin segmentation. Subdural electrodes were inserted and then full head post-insertion CT images were obtained on a GE High Speed Advantage spiral scanner with 512x512 image sizes. Three-dimensional reconstruction was also performed on the CT data with skin and electrode segmentation. The two modalities were registered in three-dimensional space using anatomical landmarks. Only the electrodes and the brain were used for visualisation of the registered data set.

Compared to the stereo-skull x-ray and paper method, we obtained three-dimensional images of specific patients' brains, showing precise locations of the electrode contacts.

P-067

Temporal Lobe Seizure Evoked by Immersion in Hot Water

G. Holloway, W. Blume (London, Ontario)

The well-documented case reports of hot water precipitated focal seizures involve the frontal temporal (Stensman and

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Ursing, 1971) and temporal occipital (Lisovoski et al, 1992) regions. Ours may be the initial case of a hot water precipitated focal seizure confined to the temporal lobes.

Routine Awake EEGs (2). Immersion in hot 40 degrees C water with video EEG and core temperature monitoring.

Immersion in hot water consistently evoked a diffuse pleasant sensation, deja vu, olfactory phenomena and a visual illusion since childhood in a 46-year-old otherwise neurologically normal male. Reproduction of the clinical stimulus of hot water produced a right temporal (T4-M2-F8) -originating seizure which gradually spread to the left temporal region. Core temperature remained constant at 36 degrees C. Repeat immersion within minutes of the first seizure failed to evoke either clinical symptoms or the electrographic ictus.

Rare precipitants of focal seizures should be sought in the history. The seizure in this patient, confined to the temporal lobes, was likely precipitated by the sensation of immersion as core temperature failed to rise during the ictus.

P-068

Topiramate in Clinical Practice - A Review of its Use in a Pediatric Epilepsy Population in Newfoundland

D.J. Buckley, M.S. Hall, S. Penney (St. John's, Newfoundland)

Background: Topiramate is a new anticonvulsant that has been available in Canada since 1997. We assessed our experience with this medication over the last 2½ years.

Methods: The Neurology Department, at the Janeway Child Health Centre, takes care of most children with refractory seizures in Newfoundland. Patients receiving Topiramate were identified from our database. This group of patients represents the following study:

Results: Twenty-six patients have received Topiramate, 15 were female and 11 were male. Age, at time of receiving Topiramate, ranged from 3 years to 18 years. Most of the patient's seizures were intractable and started within the first year of life with various etiologies being identified. All children have received at least 3 anti-convulsants prior to commencing Topiramate. The majority of children used Topiramate as add-on therapy, usually with at least 2 anticonvulsants. Side effects didn't always relate to higher dosages. The majority of children have used Topiramate for less than a year. Most experienced no side effects and most continue on therapy.

Conclusion: Topiramate has been used in a highly selected group of children with significant disabilities and intractable seizures. Topiramate appears, in the short term, to have been well tolerated and useful in this population.

P-069

Threshold of Functional Mapping Using Subdural Grid in Children

S. Chitoku, H. Otsubo, Y. Harada, V. Jay, J.T. Rutka, O.C. Snead (Toronto, Ontario)

Background: The aim of the study is to confirm that cortical stimulation can produce functional responses in children, and to investigate the roles of several factors including age pathology, and epileptic zone.

Methods: We evaluated the functional response thresholds in 19 children (2~16 years old) with refractory seizure disorders using subdural electrodes for epilepsy surgery. Pathology was divided into two groups: group A had gliosis or unremarkable change (10 patients), and group B had cortical dysplasia (9 patients). Four patients had previous operation in the same hemisphere.

Results: We succeeded to delineate motor function in all the patients. There was a tendency for younger patients to require higher amperage stimulation. Stimulating threshold was higher (3~20 mA, mean 13.08) in cortical dysplasia than group A (2-14 mA, mean 5.75). The amperage thresholds were not likely effected by epileptic zones in patients.

Conclusions: It is important to know the threshold of cortical stimulation in children to complete the safe and successful functional mapping for epilepsy surgery. The threshold of cortical stimulation in children depends on the age and pathology.

P-070

The Clinical Efficacy of Stiripentol in Refractory Epilepsy in Children

C. Deacon, M. Neveu (Sherbrooke, Québec) and P. Langevin (Québec, Québec)

Background: Stiripentol (STP) is new antiepileptic drug (AED) which has an action by inhibiting GABAand also by the potentialisation of other AEDs through the inhibition of P-450 cytochromes. Recently published data (Epilepsia, 40(11):1618-1626, 1999) suggest that STP is effective in refractory partial epilepsy and in Severe Myoclonic Epilepsy in Infancy. In our study, tolerability and efficacy of STP were assessed in many types of refractory epilepsy in children.

Method: This was an open study of STPas an add-on therapy in 14 patients with refractory epilepsy (5 patients with generalised epilepsy, 7 patients with partial epilepsy and 2 patients with Lennox-Gastaut syndrome). The dosage of STP was variable and not exceeding 90mg/kg/day. Clinical efficacy on seizure frequency and side-effects were recorded with follow-up visits, phone calls and chart review. The mean follow-up time on the drug was 3, 4 months.

Results: In the generalised epilepsy group, 3 out of 5 patients (60%) were improved by more than 50%, with 2 patients being seizure free. In the partial epilepsy group 3 out of 7 patients (43%) were improved by more than 50%, with one seizure free patient. Both patients with Lennox-Gastaut syndrome were improved by more than 90%. The side-effects recorded included somnolence, nausea and ataxia. Most major side-effects were related to drug interactions with other AEDs (phenytoin, carbamazepine, clobazam) which occurred in 4 patients.

Conclusion: Stiripentol seems to be a very promising drug as an add-on therapy in many types of refractory epilepsy. It is also relatively well tolerated but drug interactions have to be kept in mind.

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P-071

Nonconvulsive Status Epilepticus in Multiple Sclerosis

D. Dimitrakoudis, A. Guberman (Ottawa, Ontario)

Multiple sclerosis classically presents with symptoms and signs attributable to dysfunction of central nervous system white matter tracts. However, less commonly multiple sclerosis plaques may manifest their presence by causing paroxysmal phenomena such as seizures, which are attributed to focal or diffuse cortical dysfunction. Multiple sclerosis has even been implicated as a cause of status epilepticus in rare patients. However, the occurrence of non-convulsive status epilepticus due to multiple sclerosis is a little known phenomenon. Here are presented two cases of non-convulsive status epilepticus occurring in the context of previously diagnosed multiple sclerosis. As a subgroup of patients with MS and epilepsy, this group is quite rare and can be easily missed if not included in the differential diagnosis of delirium in MS patients. Included is a review of the prevalence of epilepsy in the multiple sclerosis population and a discussion of relevant pathophysiology. Since some common conditions which worsen MS symptoms also exacerbate seizure disorders (fever, infection etc.), the importance of considering non-convulsive status epilepticus in the differential diagnosis of delirium in MS patients is emphasized.

P-072

The Efficacy and Tolerability of Topiramate in Drug Resistant Partial Epilepsy – A Cochrane Metaanalysis

N. Jette, A. Guberman (Ottawa, Ontario), A.G. Marson, Z.A. Kadir, J.L. Hutton (Liverpool, United Kingdom)

Background: 30% of patients with seizures will develop refractory epilepsy. In this review, we evaluate the efficacy and tolerability of topiramate as an add-on treatment in patients with drug resistant partial epilepsy. The Cochrane methodology will be discussed along with the advantages and limitations of metaanalyses.

Methods: The following outcomes (odds ratios, OR) were assessed: (1) 50% or greater reduction in seizure frequency, (2) treatment withdrawal and (3) side effects. Intention to treat analysis was performed and dose response evaluated in regression models

Results: Six randomized controlled trials were included (743 patients). (1) Efficacy: Overall OR for 50% or greater reduction in seizure frequency compared to placebo: 4.06. Dose regression analysis showed increasing efficacy with increasing dose. (2) Global effectiveness: Treatment withdrawal OR compared to placebo: 2.57. (3) Side effects: Dizziness, fatigue, nausea, somnolence and thinking abnormally were significantly associated with topiramate.

Conclusions: Topiramate has efficacy as an add-on treatment in patients with drug resistant partial epilepsy. However, trials reviewed provided no evidence for long-term efficacy of topiramate, nor for its role in monotherapy or in other epilepsy types. Although metaanalyses have been designed to provide the most reliable evidence, rigorous methodology must be used to avoid error or bias.

P-073

Induction of Hypersensitivity to a Previously Tolerated Antiepileptic Drug by a Second Antiepileptic Drug

B.D. Klassen, R.M. Sadler (Halifax, Nova Scotia)

Background: Adverse cutaneous reactions to antiepileptic drugs occur not infrequently, ranging in severity from an isolated mild rash to a severe systemic hypersensitivity syndrome. Genetically determined abnormalities in enzymatic detoxification systems have been postulated as one cause of these reactions. Immunologic mechanisms are also felt to play an important role. Cross sensitivity has been well described, with patients developing a reaction to more than one antiepileptic drug.

Methods: Case report and review of the relevant literature.

Results: A patient is reported who was treated with phenytoin for 6 months without adverse effect, but developed a hypersensitivity reaction with rash, fever, elevated liver enzymes, lymphadenopathy, and colitis 6 weeks after the introduction of carbamazepine. Phenytoin and carbamazepine were discontinued. Seizure control was suboptimal despite treatment with valproic acid and clobazam. A decision was made to cautiously reintroduce phenytoin. Diffuse skin rash and pharyngitis appeared after 2 doses of phenytoin.

Conclusions: The antiepileptic drug hypersensitivity syndrome has been thought to occur as a consequence of pre-existing pharmacogenetic and immunologic abnormalities. Our case demonstrates induction of hypersensitivity to an antiepileptic drug that had been formerly well tolerated, following a hypersensitivity reaction to another antiepileptic drug. This is distinct from simple cross-reactivity between more than one drug. This induction of hypersensitivity with antiepileptic drugs has not been previously described.

P-074

Improvements in Language, Cognition and Seizure Control with Sulthiame in "Benign" Partial Epilepsy of Childhood

E Wirrell, N. Lowry, D Newmeyer (Saskatoon, Saskatchewan)

Purpose: To assess seizure control, language and cognitive function with of sulthiame in children with typical and atypical forms of "benign" partial epilepsy of childhood.

Methods: 13 children (mean age 8 years, range 6-12, 5 M 8 F) were treated with sulthiame (dose 5-14 mg/kg/d) over a 19 month period. Mean follow-up was 10 months (range 1-20). Sulthiame was considered in cases of refractory rolandic seizures or in subjects with language or cognitive delay whose EEGs showed benign focal sharp waves, irrespective of whether seizures were present. Clinical histories, cognitive and language assessments and EEG reports were reviewed before and after introduction of sulthiame.

Results: Overall 8/13 (62%) showed a favorable response to sulthiame. Seven of 11 (64%) children with a history of seizures demonstrated a decrease in seizure frequency (4 seizure-free). With regards to language and cognitive function, 3/6 (50%) with longstanding delay but no regression improved compared to 4/5

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(80%) with regression. All patients with Landau-Kleffner (LKS) and continuous spike-wave in sleep (CSWS) showed significant improvement.

EEGs were repeated after initiation of sulthiame in 10 patients and were improved in 8 (80%). EEG improvement tended to correlate with clinical improvement (p=0.07).

Eight (62%) continue on sulthiame (4 monotherapy). Three of 5 stopping sulthiame did so for side effects (2-irritability and hyperactivity, 1-tremor and worsening seizures) and 2 for lack of efficacy. No child continuing on sulthiame has developed adverse effects.

Conclusions: Sulthiame frequently improved seizure control, language and cognition in (1) children with atypical benign partial epilepsy of childhood with developmental regression and (2) LKS with CSWS. It may also be helpful in patients with rolandic seizures and language or cognitive delay, even without a clear history of regression.

P-075

Development of an Educational Package for Families in British Columbia whose Children have been Recently Diagnosed with Epilepsy

C. Massey (Vancouver, British Columbia)

Background: Approximately 0.5-1.0% of children in British Columbia have epilepsy, and not all of them are diagnosed by a pediatric neurologist. In order to ensure that the families receive optimal and current information about their child's diagnosis, we developed an educational package to be given to families regardless of who made the diagnosis. We have been utilizing the package at British Columbia's Children's Hospital (BCCH) since September, 1998.

Methods: A literature review was conducted and an epilepsy information package was developed. The families are given a package which contains general epilepsy information and a set of pamphlets specific to their child's age, diagnosis and medication regime. A caremap individualizes these packages. For children diagnosed outside of BCCH, a card containing the pertinent information for the child is sent by their physician to the Society who, in turn, compiles the package and sends it to the family. An evaluation tool has been sent to families who have received the package in the past year.

Conclusion: We anticipate that the above package will improve the consistency of information provided to families of children with epilepsy regardless of their geographical location or the source of their diagnosis. Preliminary evaluation results from both families and physicians have been extremely positive.

P-076

Refractory Seizures Following Functional Hemispherectomy: Important Lessons Learned from an Unusual Case

S. Mittal, J-P. Farmer, B. Rosenblatt, F. Andermann, J.L. Montes (Montreal, Quebec), J-G Villemure (Lausanne, Switzerland)

Background: Surgical failures following functional hemispherectomy occur in about 15% of individuals with catastrophic epilepsy. These are traditionally attributed to incomplete disconnection, incorrect localization of epileptiform activity, or persistent focus in the ipsilateral insular cortex.

Methods: We report the case of a 7 year-old boy with an intractable seizure disorder of classical "frontal adversive flavor" related to extensive unilateral left hemispheric cortical dysplasia.

Results: A standard functional hemispherectomy with insular cortex resection was performed. After a seizure-free period of 6 months, a new pattern ensued consisting of dystonic posturing of the right arm with a "diencephalic-like" syndrome. EEG and ictal/interictal SPECT localized the focus to the ipsilateral basal ganglia. MRI suggested that residual frontobasal tissue was dysplastic. Therefore, a resection of the epileptogenic frontal basal tissue up to the anterior commissure was completed. The patient has remained free of seizures on 15-month follow-up.

Conclusions: Standard hemispherectomy techniques provide extensive disconnection, despite the presence of residual frontal basal cortex. Rarely, especially if dysplastic, this tissue can represent a focus of refractory seizures. This is an important consideration for cortical dysplasia patients in determining the source of ongoing seizures post-hemispherectomy. It remains essential to investigate them fully before considering them refractory to surgery.

P-077

Delayed Crural Status Epilepticus: A Vestige of Bifrontal Leucotomy

Abayomi Ogunyemi (St. John's, Newfoundland)

Background: Post-operative seizures were recognized as complications of frontal leucotomy. Information is lacking about delayed epilepsy attributable to the procedure.

Methods: Neurological examinations were performed during and immediately following an episode of status epilepticus (SE) in a patient who had bifrontal leucotomy. EEG was also performed at the time of the status epilepticus.

Results: This 72-year-old man had bifrontal leucotomy when he was 28 years old. He began to have seizures ten years later. He had 2 types of seizures: (i) secondarily generalized tonic clonic seizures with post-ictal aphasia and right hemiparesis and (ii) long-lasting, repetitive, synchronous jerking of the legs unassociated with altered sensorium. The leg jerking was more prominent on the right. EEG during the SE showed secondary bilateral synchrony with recurrent high amplitude sharp waves and diffuse rhythmic delta waves predominating in the left frontal region. CT scan of the brain confirmed the bifrontal leucotomy.

Conclusion: Delayed-onset epilepsy, including status epilepticus involving both legs, is another untoward effect of the discredited neurosurgical procedure of bifrontal leucotomy.

P-078

Motor Vehicle Driving and Epilepsy in the New Century

G.M. Rémillard, F. Andermann, B.G. Zifkin (Montréal, Quebec)

We suggest some useful policies for regulating driving by patients with epilepsy and without progressive brain lesions.

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Classes of motor vehicle permits would be uniform internationally. Suspension and limitation of driving privileges is a role of government and not physicians. Before obtaining a permit or a new class of permit, or when renewing a permit, the driver must inform the licensing body of health problems, as outlined in a written document given to all drivers. The responsible individual has the legal obligation to self-report any such health problems to the licensing body as they arise between license renewals. The physician may report patients who do not comply or who are otherwise judged to be dangerous drivers for medical reasons, with immunity from prosecution, and must inform the patient of the patient's obligation to report such health problems. It is the responsibility of the physician to complete standardized forms issued by the licensing body. Significant items should be described by the physician in adequate detail to allow the authorities to reach an informed decision for each applicant. Guidelines should be published describing necessary seizure-free intervals for epilepsy, and other conditions which must be met for each class of permit.

Some exceptions for epilepsy may allow shorter seizure-free intervals for some classes of permit: Attacks exclusively during sleep, or shortly after awakening without prolonged postictal impairment when the pattern has been established for one year; non-incapacitating simple partial attacks and prolonged aura without incapacitating features when the pattern has been established for one year; isolated seizure after a prolonged seizure-free interval (at least two years); seizure recurrence after modification of treatment on medical advice, when seizures have been controlled for a long period (usually more than two years); exceptional precipitating circumstances that are not likely to recur, in a patient with epilepsy; a single seizure with a positive EEG provided treatment is started; detailed medical report with special or compensating circumstances.

P-079

Seizures Originating From and Resections In the Second Sensory Area: A Report of Two Cases

R. Sahjpaul, S. Wiebe, W. Blume, C. Kubu, P. Derry (London, Ontario)

Background: Second sensory area seizures are very uncommon as are resections in this area. We report two illustrative cases.

Methods: The first is a case of a 31 year-old right handed male with medically resistant seizures originating from the dominant second sensory area, occurring up to 100 times daily. No lesion was demonstrated on MRI. After invasive monitoring he underwent partial resection of the dominant supramarginal gyrus without permanent language or other deficit. The second case is that of a 39 year-old right handed woman with a left inferior rolandic cavernous angioma causing seizures. Perisylvian lesionectomy and cortisectomy were performed with no immediate post-operative deficits.

Results: The first patient remains well at 2 year follow-up with less than 10 seizures daily. The second patient developed delayed onset (3 weeks post-op) unusual sensory complaints with aberrations in taste and impaired temperature sensation in her mouth and bilateral extremities without objective deficit. The symptoms are slowly improving 18 months later.

Conclusion: Seizures from and resections in the second sensory area are uncommon. These cases illustrate the unusual symptom complex associated with lesions in this area.

P-080

Does Response of Initially Resistant Partial Epilepsy Relate to the Mechanism of Action of the Subsequently Effective Drug?

J. Spencer, C. Corman, A. Guberman (Ottawa, Ontario)

Background: Thirty percent of patients with epilepsy have intractable seizures that often require polytherapy. We studied a group of patients with intractable seizures to determine whether their eventual response to an antiepileptic drug (AED) might depend on a different mechanism of action (M.O.A.) from previously tried ineffective AEDs.

Methods: This retrospective chart review included forty-three patients from an epilepsy clinic with initially unresponsive seizures who eventually responded to an AED. The seizure frequency, drug history, M.O.A. of each drug and serum drug levels were recorded for each patient.

Results: Of the twenty five patients who met the inclusion criteria, thirteen (52 percent) achieved seizure control with an AED of a different M.O.A. from previously tried AEDs. The mean number of AEDs tried before control was achieved was 6 and patients required 2-3 concomitant AEDs to maintain seizure control. Trends were observed for specific seizure types, regarding which new and traditional AEDs were most likely to achieve seizure control.

Conclusions: Adding on or switching to an AED with a different M.O.A. was an effective approach in half of the difficult-to-treat patients. However an equal number of patients responded to an AED with a similar M.O.A. to previous drugs. M.O.A. may play a role in determining subsequent drug selection in patients with intractable seizures. Future work in this area should include a prospective trial.

P-081

Tiagabine in Intractable Epilepsy - A Clinical Practice Experience in the Quebec City Area

S. Verreault, P. Langevin, R. Desbiens (Quebec City, Quebec).

Background: Tiagabine is effective as add-on therapy for partial seizures in patients with refractory epilepsy. Tiagabine is available on a compassionate basis in Canada. We assessed the efficacy and safety of tiagabine for a group of pediatric and adult patients with intractable epilepsy in our clinical practice.

Methods: All patients treated with tiagabine at the two study centers between January 1998 and December 31, 1999 were analyzed retrospectively. Data were gathered on base-line characteristics of patients, seizure response and medication related adverse events.

Results: Thirty-five patients were treated with tiagabine. The results were strikingly different in the two study centers. The mean duration of follow-up was 124 days. Over 90% seizure

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reduction was achieved in 4 (11%) patients, 50%-90% in 6 (17%), and 50% in 5 (14%). Tiagabine was stopped in 20 (57%) patients. In 4 (11%) patients tiagabine was stopped because of a deterioration in seizure control, in 6 (17%) because of medication related adverse events and in 10 (29%) for poor response.

Conclusions: Although tiagabine resulted in 50% seizure reduction in 10 (29%) patients of this group of patients with previously intractable epilepsy, it had harmful effects in 10 (29%) patients that led to its discontinuation.

P-082

Gap Junctional Communication is Upregulated by Seizures Induced by Repetitive Tetanization or Bicuculline in Hippocampal Slice Cultures

K. Wentlandt, Y. Adamchik, J. Li, J.L. Perez Velazquez, P.L. Carlen (Toronto, Ontario)

Background: Increasing evidence suggests that gap junctional communication between cells plays a significant role in neuronal synchrony and in the generation of some seizure types. Using a simplified, organized *in vitro* mammalian CNS system, we examined the hypothesis that gap junctional function and expression is increased following seizure induction.

Methods: Hippocampal slice cultures were prepared from 7 day old Wistar rats. Experiments were performed after 7 days in culture.

Results: Bicuculline (10μM) was added to the medium for 16 hours during which time seizure activity was noted electrophysiologically from the CA1 area. These seizures were attenuated by gap junctional blockers and were associated with markedly increased immunohistochemical staining for connexins 32 and 43.

Another seizure model entailed the use of repetitive tetanization of the CA3 to CA1 connections, creating primary epileptic afterdischarges in hippocampal slice cultures. Fluorescence recovery after photobleaching (FRAP), a measure of gap junctional communication by the passage of fluorescent dye between cells, was significantly enhanced once seizures were established. In this preparation, FRAP is greatly decreased by gap junctional blockers such as carbenoxolone and octanol.

Conclusions: Gap junctional communication may play a significant role in the generation of seizure activity.

P-083

Intra-operative Mapping of Brain Motor Speech Areas

W.B. Woodhurst, C. Reddy (Vancouver, British Columbia)

Background: Intra-operative stimulation mapping using varying stimulation and recording methods has been employed to define eloquent cortex during surgical treatment of intracerebral lesions and epileptogenic foci. This report reviews results of inferior posterior frontal lobe stimulation in a series of 34 patients.

Methods: Most procedures were performed for temporal lobe epilepsy. Cases with inadequate frontal exposure, inadequate exploration or inadequate diagrams (5) were omitted from analysis for presentation. Intra-operative stimulation mapping employed 60 Hz biphasic square wave controlled current application with control electrocorticography.

Stimulation responses were recorded intra-operatively on brain map diagrams. Intra-operative photographs where available were used to cross check diagrams.

Results: The speech arrest responses without overt or reported motor activity response in tongue, face or throat regions were pars opercularis 11, low precentral (rolandic operculum) 4, pars triangularis 2. Maps presenting the responses in each region will be presented.

Conclusions: The motor speech cortex, defined as that region producing speech arrest without motor or sensory responses, mapped with this protocol appears more restricted than in other reports of intra-operative stimulation mapping. This may be due to use of the anatomic diagram for recording and other technical or methodological factors.

P-084

Medical Guidelines for the Employment of Individuals with Epilepsy or Isolated Seizures in Safety Critical Positions in the Railway Industry

C. Lapierre, F. Andermann, C. Laberge-Nadeau, G.M. Rémillard, B.G. Zifkin (Montreal, Quebec)

Railroad employees with epilepsy who work in safety critical positions (SCP) are responsible for the movement of trains as defined in the Railroad Safety Act (1982). It is required that their epilepsy be controlled.

We suggest that for this purpose, controlled epilepsy be defined as:

- In the case of epilepsy treated at any time with AEDs only: A period of 5 years without seizures with or without medication at the time of ascertainment *and* absence of epileptiform activity in serial EEGs performed over a period of 5 years and interpreted by a certified electroencephalographer.
- In the case of epilepsy due to a non progressive lesion which has been treated surgically: A period of 5 years following surgery, on medication, without seizures *and* absence of epileptiform activity in serial EEGs performed over a period of 5 years and interpreted by a certified electroencephalographer.
- Seizures always related to sleep without postictal impairment during wakefulness treated with AEDs, and in which this clinical pattern has been present for at least 5 years at the time of evaluation.
- Auras or strictly simple partial seizures including isolated auras, without significant cognitive, sensory, or motor impairment, which occur even with AED treatment in a stable pattern established for at least 5 years.

Monitoring requirements, medical assessment, and follow-up for patients after withdrawal of epileptic drugs should be defined.

A first seizure with epileptiform EEG activity, single unprovoked or isolated seizures, and acute symptomatic seizures (provoked seizures or neighbourhood seizures) should be evaluated using the guidelines that apply to employees with epilepsy holding SCP and each situation must be evaluated individually before determination of assignment to duties.

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NEURO-ONCOLOGY

P-085

Central Hypoventilation, Ataxia and Diabetes Mellitus in a Patient with a Bronchial Carcinoma; an Unusual Combination of Paraneoplastic Disorders

C. Bocti, P. Duquette, H. Masson. (Montréal, Québec)

Background : Central hypoventilation and gait ataxia have been described in association with paraneoplastic brainstem encephalomyelitis (PBEM). Diabetes mellitus has not been associated with PBEM. We describe a case in which these three features were present in a patient with a bronchial carcinoma.

Case report: A 52-year-old man presented with a 12-week history of diplopia, dysarthria, gait ataxia, and drowsiness. He had been diagnosed with insulin-dependent diabetes 4 weeks before admission. On admission he had multi-directional nystagmus, dysarthria and gait ataxia. During the first admission day, the patient was found unarousable and bradypneic with severe hypercapnia and hypoxia. He was intubated and ventilated. Brain MRI was normal. CSF analysis showed a mild lymphocytic pleocytosis with moderately elevated proteins. A bronchoscopy revealed a left bronchial carcinoma, which was surgically removed. Treatment included plasmapheresis and intravenous immunoglobulins. The diabetes disappeared and ataxia improved. Respiratory assistance remained necessary.

Conclusions: This the first report of paraneoplastic central hypoventilation, ataxia and diabetes mellitus occurring together in a patient with a bronchial carcinoma. Antibodies directed against tumoral antigens presumably cross-reacted with cerebellum and brain-stem antigens; we speculate that certain antibodies could have been directed against glutamic-acid decarboxylase to explain the simultaneous appearance of ataxia and diabetes.

P-086

Influence of Aggressive versus Conservative Treatment on the Clinical Outcome and Functional Performance of Patients with Primary Malignant Brain Tumours

Miguel Bussière, Teresa Neves, Alicia Paris Pombo, Wilma Hopman, Francisco Espinosa (Kingston, Ontario)

Background: Current treatment of malignant gliomas includes surgery, radiotherapy and chemotherapy. We compared the effect of aggressive vs. conservative treatment on patient functional status and survival.

Methods: Retrospective review of 143 patients with malignant gliomas. Patients were grouped according to age, histopathological diagnosis and treatment. Patients received either, full (dexamethasone, surgery, radiotherapy and chemotherapy), partial (dexamethasone, various combinations of surgery, radiotherapy or chemotherapy), or conservative treatment (dexamethasone biopsy). Patients were assigned a Karnofsky performance score (KPS) at the time of diagnosis and at 1, 3, 6, 9 and 12 months, and yearly afterwards. Data were analyzed using descriptive analysis, Cox survival analysis and multiple linear regressions.

Results: Patients were on average 60 years old, 84 were male and 59 female. 107 patients had glioblastoma multiforme, 23 anaplastic astrocytoma and 13 anaplastic oligodendroglioma. 29 patients received full treatment, 83 partial and 31 conservative therapy. Significant differences in survival up to one year were detected using a Cox survival analysis. Mean survival times were 2.5 months (95% confidence interval, 1.7, 3.3) for conservatively-treated patients, 17.0 months (10.4, 23.6) for partially-treated patients and 33.4 months (19.3, 47.5) for patients receiving full treatment. Factors associated with survival within the first year and slower deterioration of KPS within the first 3 months after diagnosis were identified. Significant treatment complications occurred in 32.9% of patients.

Conclusions: Aggressive multimodal treatment of malignant gliomas may prolong both patient survival and functional status.

P-087

Pediatric Extraventricular Neurocytoma

C. Chaalala, J. Paquet, A. Turmel (Québec City, Québec)

Neurocytoma is classically a supratentorial neuronal tumor that arises in the lateral or third ventricle. We present a case of an unusual extraventricular neurocytoma arising in the frontal region.

A 12-year-old boy presented with seizures. An MRI disclosed a left frontal polar lesion with ring enhancement. Surgery was undertaken and total resection obtained. Histological findings confirmed a neuronal origin with a diagnosis of atypical neurocytoma.

Radiological and histological diagnosis will be discussed in depth. Prognosis and possible adjuvent therapy will be entertained.

P-088

Recurrent Pediatric Meningioma

C. Chaalala, J. Paquet, A. Turmel (Québec City, Québec)

Pediatric meningiomas are very unusual in the first two years of life.

We present a case of a child (22 months of age) who presented with a huge mass in the sylvian fissure. Signs of increased intracranial pressure were the dominant clinical finding. At operation, no dural attachment was found. A diagnosis of atypical meningioma was obtained. Total resection was confirmed by MRI post-op. One year follow-up showed recurrent multifocal meningioma. A second intervention was undertaken again with a normal post-op MRI.

Histology and prognosis will be discussed.

P-089

Meningeal Melanocytoma of the Planum Sphenoidale: Report of a Case and Review of the Literature

M. Chow, D.B. Clarke, W. Maloney, V. Sangalang (Halifax, Nova Scotia)

Background: Meningeal melanocytoma is a rare benign

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primary melanotic tumour of the meninges, most commonly found in the spinal canal and the posterior fossa.

Method/Results: We report the thirteenth case of a supratentorial meningeal melanocytoma and the first case reported to arise from the planum sphenoidale. The patient's presenting symptoms were characteristic of a large bifrontal lesion and included headaches, personality change, lethargy and urinary and fecal incontinence. CT and MRI studies showed an extra-axial tumour arising from the planum sphenoidale. The patient underwent successful gross total removal of the lesion without neurological sequelae.

Conclusion: Based on this case report, meningeal melanocytoma should be included in the differential diagnosis of extra-axial lesions arising from the planum sphenoidale.

P-090

Brainstem Gliomas: A 10-year-Institutional Review

J.-P. Farmer (Montréal, Québec)

Background: Brainstem gliomas, although rare in incidence, traditionally represent a devastating problem for young children. Have technological advances of the last decade had an impact on this disease?

Methods: Case records of 37 patients with brainstem glioma treated at The Montreal Children's Hospital from June 1989 to June 1999 were reviewed. Age, clinical evolution, radiological appearance, type of surgery practised, histological diagnosis, adjuvant treatments, and survival were analysed.

Results: 15 patients had the so-called "black pons" diagnosis and 22 patients other forms of brainstem gliomas. At the time of follow-up, disease-free survival following active treatment was 8 times longer in the group of patients not exhibiting a black pons. A non-pontine brainstem location, a cystic or exophytic component, bright enhancement with gadolinium injection, histological diagnosis of pilocytic astrocytoma or ganglioglioma were favourable prognostic factors. The relative impact of radical surgery and/or radiotherapy on morbidity and mortality is analysed.

Conclusion: Surgery coupled to adjuncts such as neuronavigation, intra-operative ultrasound, electrophysiological monitoring plays an important role for non-black pons brainstem lesions. Focal or conformal radiotherapy has an adjuvant role at the time of disease progression for this group. Little progress has been made in the management of the classical black pons glioma.

P-091

Survival, Cure Rates, Prognostic Factors and Frequency of "Collin's Law Violators (CLVs)" in Medulloblastoma in Southern Alberta

P. Federico, K.L. Young, N.B. Rewcastle, P.M.A. Brasher, P.A. Forsyth. (Calgary, Alberta)

Background: We performed this study to determine survival, "cure rates", prognostic factors, and the frequency of CLVs in an unselected population.

Methods: Using the Alberta Cancer Registry, we identified 51 medulloblastoma patients (33 male, 18 female) from 1975-96.

Results: The crude incidence rate was 0.216/100, 000. All patients underwent surgery [gross total resection (GTR) in 16, radical subtotal resection (RSTR) in 18, subtotal resection in 15, and unknown in 2], 50 received radiotherapy, and 16 received chemotherapy. Median 5 year survival was 65% for adults and 48% for children. Survival curves did not "plateau" after 5 years. Median time to progression was 4 years and median survival post-relapse was 1.2 years. Three (6%) patients were CLVs (recurrence after 13-17 years). Multivariate analysis found only GTR and RSTR were associated with long survival.

Conclusions: Survival is poor in medulloblastoma patients, "cure" is uncommon, and GTR/RSTR significantly prolongs survival. CLVs are not rare and recurrent tumor is the cause of progressive symptoms in these patients. These data highlight the need for more effective medulloblastoma therapies.

P-092

The Farnesyl Transferase Inhibitor SCH66336 Inhibits the Growth of Human Astrocytoma Cell Lines and Xenografts Implanted in NOD-SCID Mice

M. Feldkamp, L. Nelson, A. Guha (Toronto, Ontario)

Background: Our previous studies have demonstrated that glioblastoma multiforme (GBM) tumor specimens and derived cell lines express elevated levels of activated Ras-GTP, despite the absence of activating Ras mutations. Farnesyl transferase inhibitors (FTIs) appear to exert their effect in part through inhibition of Ras-mediated signaling. We have previously demonstrated that the FTI L-744, 832 inhibits the growth of astrocytoma cells through a combination of anti-proliferative, pro-apoptotic, and anti-angiogenic effects. SCH66336 is a potent FTI presently undergoing clinical trials in patients with solid tumors.

Methods/Results: We evaluated the efficacy of SCH66336 against a panel of 5 established astrocytoma cell lines, as well as against 2 human GBM tumor xenograft models in immunocompromised NOD-SCID mice. SCH66336 demonstrates an anti-proliferative effect against established cell lines (IC50 range from 7.1 μM in U87 to 32.3 μM in U373 cells). The anti-proliferative effect of SCH66336 appears to correlate with the Ras isotype expression level, with the most sensitive cell line (U87) expressing large amounts of H-Ras, and lesser amounts of K- or N-Ras. SCH66336 also demonstrates potent efficacy against human GBM tumors implanted subcutaneously in NOD-SCID mice. When dosed at 50 mg/kg po BID for 20 days, SCH66336 demonstrates a mean growth inhibition of 56% in one of the models (n=11), and a mean growth inhibition of 67% against a second xenograft model (n=17).

Conclusions: These studies demonstrate that SCH66336 is a potent novel targeted chemotherapeutic agent effective against GBM, and further studies leading to clinical trials appear to be warranted.

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P-093

Large Invasive Pituitary Adenomas: Management Strategies

F. Gentili, P. Gullane, D. Brown, J. Irish, R. Fleming

The management of large invasive pituitary adenomas remains a serious clinical problem. We report on a series of 35 patients with large adenomas (>5 cm) treated between 1982-1999. All tumors were histologically benign and exhibited extensive involvement of the sphenoid and clivus with significant supra and infrasellar extension and cavernous sinus invasion. Age ranged from 37 to 78 years with 68% female. All patients were symptomatic from neural and/or endocrinopathy. Management strategies utilized have included surgery (craniotomy, transphenoidal, mid-face and combined skull base approaches), pharmacotherapy, (bromocryptine, sandostatin, etc.), radiotherapy (conventional, stereotactic) and a combination of the above. Average follow-up has been 7.3 years. Two patients have died of their disease. All remaining patients are alive with residual disease. Symptomatic recurrence has occurred in 24% of patients requiring re-operation. Quality of life assessment revealed that 90% of patients are fully functional. In conclusion surgery is rarely curative in large invasive pituitary adenomas. A multi-disciplinary and multi-modality approach that includes surgery, medical and radiotherapy offers the best chance of long term tumor control and functional survival in this group of patients.

P-094

Loss of NF1 Causes Activation of Ras/MAPK and PI3-K/Akt Signaling in NF1-associated Astrocytoma

N. Lau, M. Feldkamp, L. Roncari, A. Loehr, A. Guha (Toronto, ON) D. Gutmann (St. Louis, Missouri)

Background: Type 1 neurofibromatosis (NF1) is an autosomal dominant transmitted cancer predisposing syndrome. The NF1 gene encodes a protein termed neurofibromin, which has been reported to possess tumor suppressor function, largely but not exclusively through its role in the negative regulation of Ras-GTP. Sporadic astrocytomas are not characterized by NF1 mutations, and frequently express elevated levels of neurofibromin. A small number of NF1 patients, however, develop astrocytomas. While loss of neurofibromin has been implicated in the molecular pathogenesis of other NF1-associated malignancies, there is no formal evidence supporting a similar role in the pathogenesis of NF1-associated astrocytomas.

Methods/Results: In this study, we report on a case of NF1-associated astrocytoma in which both tumor tissue and corresponding non-neoplastic white matter from the same patient are available for analysis. We demonstrate loss of neurofibromin expression in the tumor but not in the normal white matter, associated with loss of heterozygosity at the NF1 locus in the tumor. Levels of Ras-GTPwere considerably higher in the tumor than in the corresponding normal tissue, and there was evidence for activation of downstream signaling through the Raf-MAPK and PI3-K-Akt signaling pathways in the tumor specimen.

Conclusions: These results thus support a role for neurofibromin loss in the molecular pathogenesis of NF1-associated astrocytoma, differentiating it from the pathogenesis of sporadic astrocytomas. In addition, we demonstrate for the first time that loss of neurofibromin directly results in Ras activation in NF1-associated astrocytoma.

P-095

Ventriculoscope Tract Recurrence after Endoscopic Biopsy of a Pineal Germinoma

C. Haw, P. Steinbok (Vancouver, British Columbia)

Background: Recurrence along an endoscope tract has been described after endoscopic biopsy and resection of malignant tumors arising in the pulmonary, gastrointestinal, urologic, and gynecological organ systems. We describe the first reported case of tract recurrence following the ventriculoscopic biopsy of a central nervous system tumor.

Methods: A retrospective review of the patient's clinical course, radiology, and pathology was undertaken to formulate a case report.

Results: A fourteen-year-old boy presented with Parinaud's syndrome. Neuroimaging showed an enhancing, calcified pineal mass associated with marked hydrocephalus. He was treated with endoscopic third ventriculostomy and endoscopic biopsy of the tumor. The pathology was germinoma. Persistent hydrocephalus required repeat third ventriculostomy. The patient subsequently received focal external beam radiotherapy. Seventeen months after the first third ventriculostomy, a routine MRI revealed a two cm enhancing mass in the ventriculoscope tract. This was removed via a right frontal craniotomy. Again the pathology was germinoma. Serum and CSF markers were negative at initial presentation and at the time of the recurrence.

Conclusion: The potential for tract recurrence and CSF dissemination should be considered following the endoscopic biopsy of pineal germ cell tumors, as this could affect the extent of radiotherapy and/or chemotherapy.

P-096

Pituitary Carcinoma: A Rare Aggressive Neoplasm

E. Kachur, RL Sahjpaul (London, Ontario)

Background: Pituitary carcinomas are extremely rare neoplasms with less than 60 cases reported in the literature. The diagnosis requires the presence of craniospinal and/or systemic metastases. We present only the second reported case of a gonadotropic pituitary carcinoma.

Methods: The patient is a 46-year-old male with a 2 month history of headaches, nausea, vomiting and a third nerve palsy. Subtotal removal of an aggressive pituitary null cell adenoma by a transphenoidal approach was performed followed by focal radiation treatment with 5400 cGy in 30 fractions. The patient presented 6 months later with a C7 radiculopathy. Regrowth of the pituitary lesion was seen along with metastatic spread to the spine, liver and lymph nodes. Biopsy of the L2 vertebral body showed a FSH gonadotrophic pituitary metastatic lesion.

Results: Despite a trial of chemotherapy the patient died three weeks later.

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Conclusion: Our case showed similarities to the other reported pituitary carcinomas. The majority of patients die within one year, with no effective treatment available. Aggressive pathological features of the primary pituitary tumor may predict future likelihood of metastatic disease. Also, gonadotropic lesions appear to be a particularly malignant subtype of pituitary carcinoma.

P-097

Development and Validation of a Quality of Life Questionnaire for Patients with Pituitary Adenoma

P. Kan, M. Cusimano (Toronto, Ontario)

Background: To develop and validate a self-administered questionnaire for measuring the health-related quality of life (HRQOL) of patients with pituitary adenoma.

Methods: Literature review and focus group interviews with 9 patients, 2 family caregivers, 2 RNs, and a neurosurgeon were used to develop the 106 item content of questionnaire Version 1.0. This questionnaire was mailed to 20 patients, and the 30 most important items ranked by the patients with 17 additional items considered important by health care professionals, constituted Version 2.0 of the questionnaire. For validity and reliability assessment, Version 2.0 was mailed to 55 patients. Concurrent validity was assessed by Pearson correlation coefficients between subscales of Version 2.0 and subscales of RAND36, FACT-G, and the Karnofsky Scale. Version 2.0 scores in extreme groups defined by the Karnofsky scores were compared by a T test. Test-retest reliability, a month apart, was determined by the Pearson correlation coefficient and a T test between the two sets of scores.

Results: 47 patients (85.5%) returned completed Version 2.0. Concurrent validity for each of the subscales with RAND and FACT-G were: General Health (0.62, 0.77), Social/Family Well-Being (0.52, 0.36), Emotional Health (0.62, 0.54), and the Karnofsky Scale (0.75). Extreme groups were significantly different (15.66, 23.12, $p = 0.011$). Test-retest reliability ($n = 24$) was 0.88. Scores 1 month apart were not significantly different (21.42, 20.68, $p = 0.73$). Patients recommended that 7 items be dropped from Version 2.0.

Discussion/Conclusions: A patient-centered HRQOL questionnaire developed for patients with pituitary adenoma was shown to have good evidence for validity and reliability.

P-098

Benign Pituitary Adenoma with Multiple Dural Metastases and Negative P53 Immunohistochemical Staining, A Case Report

Krishna Kumar (Regina, Saskatchewan), Michael Kelly (Saskatoon, Saskatchewan)

Background: We present a case report of a benign pituitary adenoma with multiple dural metastases without malignant transformation. The authors believe this is the fourth reported case of this type in the literature. The tumor lacked immunohistochemical evidence of p53, throughout its course, which is a rare phenomenon. The role of p53 has been well established in the diagnosis of pituitary carcinoma.

Clinical presentation: A 38-year-old male presented with pituitary adenoma, with visual disturbance and cranial nerve palsies. Initially he underwent a transphenoidal and when it recurred a transfrontal excision was performed. He subsequently developed multiple dural-based metastases. In spite of the aggressiveness of this tumor, there was absence of p53 immunohistochemical staining which is usually used as a biomarker of aggressiveness and malignant transformation of pituitary adenomas to pituitary carcinomas.

Conclusion: Failure to demonstrate increased p53 immunostaining does not ensure a favorable outcome in pituitary adenoma. Possibly, there are yet unknown factors, which will be discussed, which contribute to malignant transformation. The treatment in such cases remains palliative.

P-099

Glioblastoma Multiform with Long Survival

N. Khairallah, R. Moumdjian, J-P. Bahary, K.Bélanger, F. Berthelet, J. Leasage (Montreal, Quebec)

We reviewed the cases of Glioblastoma multiform (GBM) we encountered at our center over a period of ten years; we found six unusual cases of long survival of more than five years. This personal series was reviewed in according to clinical, radiological and pathological characteristics.

All patients were young, with age varying between thirty-three and forty-seven years on diagnosis. All of them had a karnowsky over fifty on diagnosis. All patients had cerebral CT-scans and MRI. All patients had gross total resection except for one who had only a stereotaxic biopsy. Another case was shunted for hydrocephalus and gross total resection. All patients received complete treatment of radiotherapy and chemotherapy. We did not find any radiological characteristics for these cases. On pathology studies, we found one case of polymorphic xanthoastrocytoma that degenerated into GBM, one malignant ependymoma of the temporal lobe, three grade four gliomas (Dumas-Duport) including one cerebellar GBM and one grade three glioma. Amongst these high-grade glioma, we found two cases that had minor oligodendroglioma components.

A young age, a good karnowsky on diagnosis, a gross total resection, a full treatment of radiotherapy and chemotherapy and oligodendroglial components seem to confer good prognosis for GBM cases.

P-100

Intracranial Ependymoma with Extracranial Metastasis: A Case Report

A.Nataraj, F.Gentili, W.Halliday (Toronto, Ontario)

Metastasis of intracranial tumors outside the central nervous system is rare, occurring in approximately 1% of cases. Ependymomas are tumors derived from ependymal cells, and are more common in children than adults. When metastatic, they usually seed along cerebrospinal fluid axes. We report a case of an intracranial ependymoma with extracranial metastases.

A 33-year-old man presented with headaches, and was found

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to have an intraaxial frontal brain tumor which was resected and discovered to be an anaplastic ependymoma. He was treated with radiotherapy. The tumor recurred intraaxially and was again resected. He was treated with chemotherapy. He had three subsequent recurrences over the next two years treated with resection, and the most recent recurrence was accompanied by a mass in the scalp and several neck masses. He underwent repeat craniotomy and modified radical neck dissection. The pathology showed anaplastic ependymoma in the brain, temporalis muscle, and neck.

There are few reported cases of metastatic ependymoma in adults, with most arising from the sacro-coccygeal area. Previous craniotomy has been suggested as a risk factor for extracranial metastases of intracranial tumors, and may account for extension in our case. This and other possibilities, and a brief literature review are presented.

P-101

Primary Leptomeningeal PNET

J. Paquet, C. Chaalala, A. Turmel (Québec City, Québec)

PNETs are common lesions in the pediatric population. They are found principally in the posterior fossa (medulloblastomas) or less often in the supratentorial region.

We present the case of a child (10 years old) who presented with signs of meningismus. MRI demonstrated diffuse leptomeningeal enhancement with gadolinium in the supra-, infratentorial region and in the spinal cord. A primary diagnosis of meningitis was entertained but rapid evolution prompted a CSF diversion and leptomeningeal biopsy.

Histology revealed a PNET. Adjuvent therapy with radiotherapy and chemotherapy (POG protocole 9631 - 3 cycles of cysplatin, VP16 and 8 cycles of high dose cyclophosphamide and vincristine) was given.

Partial response was obtained.

Follow and prognosis will be discussed.

P-102

Glioblastoma Multiforme (GBM) Arising in the Field of Gamma Knife Radiosurgery for Vestibular Schwannoma: Case Report and Review of the Literature

A. Shamisa, M. Bance, W. Halliday, C. Tator, S. Wong, A. Guha (Toronto, Ontario)

Background: Stereotactic radiosurgery (SR) is being increasingly advocated as the primary modality of treatment for vestibular schwannomas. SR has been shown to arrest tumor growth with only a few associated short-term morbidities, and provides better facial nerve and hearing preservation rates than microsurgical removal. However, the long-term potential tumorgenic complications of converting a benign schwannoma to a malignant one, or inducing a secondary malignancy, are not known.

Methods/Results: We report a case of a 2.9 cm vestibular schwannoma in a non-NF2 patient who underwent Gamma Knife treatment 7 yrs ago. Within a few months post SR she required tumor removal due to progressive hydrocephalus. She subsequently presented with symptoms of raised ICP. Imaging demonstrates a new ring enhancing lesion in inferior temporal lobe adjacent to the radiation field. This lesion was pathologically confirmed as GBM.

Conclusions: This case fulfills the criteria of a radiation-induced secondary neoplasm: 1- Two different pathologically proven neoplasms; 2- The secondary arising in the field which would receive scatter radiation; 3- A long enough latency of 7 years. Although this first case report of GBM after SR does not conclusively prove a causal relationship, it does illustrate that we should be more vigilant of these long-term, rare, but potentially lethal complications of SR. We will critically discuss the literature where there are a few reports of malignant vestibular schwannomas with a high correlation with prior SR. We hope this report will stimulate further interest in examining the consequences of SR.

P-103

Hereditary Posterior Fossa Tumours in a Family with a Truncating Germline Mutation of *hSNF5*

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Background: CNS rhabdoid tumours, renal rhabdoid tumours and medulloblastomas are all known to have a high incidence of loss of heterozygosity on chromosome 22q11. Recently, the *hSNF5* gene on chromosome 22q11 was found to be deleted in a series of renal rhabdoid tumours. The mechanism whereby loss of expression of *hSNF5* leads to malignancy is unknown.

Methods: We have identified a family afflicted by posterior fossa tumours of infancy including medulloblastoma and choroid plexus carcinoma. After obtaining IRB permission and informed consent from family members, peripheral blood samples were collected so that RNAand DNAcould be extracted. Using PCR, RT-PCR and sequencing, we performed a mutational analysis of the *hSNF5* gene in this family as a possible cause for the high incidence of malignancy observed.

Results: We have identified a truncated *hSNF5* cDNA transcript from leukocyte cDNA from affected family members, some unaffected family members as well as tumour cDNA. Sequencing of this abnormal transcript revealed fusion of exon 6 to exon 8. Subsequent sequencing of exon 7 and surrounding intronic sequences from genomic DNA revealed a splice site mutation G-Ain the 3'splice site of exon 7. This mutation affects the conserved splice site recognition site for exon 7 and accounts for the loss of exon 7 in the mature cDNA. This mutation (loss of exon 7), results in a frameshift and generation of a premature stop codon.

Conclusions: We have identified a family with a high incidence of posterior fossa tumours of infancy who have a germline mutation in the tumour suppressor gene *hSNF5*. This suggests that germline *hSNF5* mutations predispose to a novel autosomal dominant syndrome with incomplete penetrance of familial pediatric brain tumours. Families with a high incidence of pediatric brain tumours may have germline *hSNF5* mutations.

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P-104

Aberrant G-Protein Signalling in Neural Tumors

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Background: We discuss aberrancies in GTP binding protein (G-protein) signalling pathways in the molecular pathogenesis of four neural tumors: 1) Astrocytomas- sporadic and neurofibromatosis1 (NF1) associated; 2) Neurofibromas- sporadic and NF1 associated; 3) Tuberous Sclerosis (TSc) giant cell astrocytomas; 4) Pituitary adenomas. G-proteins are involved in a number of signalling pathways emitting from cell surface receptors that regulate cellular mitogenic responses to extracellular stimuli.

Methods/Results/Conclusions: Human astrocytomas have elevated levels of the activated G-protein Ras, without primary oncogenic mutations. In sporadic astrocytomas this is due to increased signals from overexpressed or constitutively activated growth factor receptors, while in NF1 astrocytomas it is secondary to decreased neurofibromin which functions to inactivate Ras. Lack of neurofibromin also leads to increased Ras activity in sporadic and NF1 associated neurofibromas and neurogenic sarcomas. Half of TSc patients have a germline mutation in the TSc2 gene which encodes for tuberin, an inactivator of another small G-protein called Rap1B which in-turn is involved in regulation of Ras. TSc associated giant cell astrocytomas lack tuberin, and the majority of sporadic astrocytomas have either loss of tuberin or overexpression of Rap1B. Lastly, a substantial subset of pituitary adenomas show constitutive activation of the G-alpha subunit of the heterotrimeric large Gs-protein, involved in transmitting signals from many hormonal receptors such as the growth hormone receptor, leading to increased cytosolic levels of cyclic-AMP, resulting in aberrant mitogenic signals. These findings will lead to better targeted therapies for these tumors.

GENERAL NEUROLOGY

P-105

Quantification of the Severity of Fatigue in Post-polio Patients

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Background: Although fatigue is common and highly debilitating in many post-polio survivors, its nature is poorly characterized and its severity difficult to quantify. To measure the efficacy of any new treatment, a measurement tool with proven sensitivity and reliability must first be established.

Methods: A fatigue questionnaire, the Revised Piper Fatigue Scale (RPFS), initially developed for cancer patients, was used to quantify the symptoms of fatigue in post-polio patients. The questionnaire consists of 22 items, each quantified on a Likert scale of 0 to 10, covering 4 different dimensions of fatigue: behavioral, affect, sensory, and cognitive/mood. The questionnaire was completed to report general feelings of fatigue as well as variations in its patterns throughout the day. The variations were assessed by filling out the questionnaire three times a day on Sunday and Monday for a two-week period. 4 patients – women between the ages of 49 and 67 years – were compared with 6 normal subjects. Each subject was also screened for depression using the Beck Depression Inventory.

Results: None of the subjects were clinically depressed. Within and between group differences were analyzed using the student t-test. The post-polio patients were significantly more fatigued than the normal controls ($p<0.001$), in general and throughout the day, particularly in early afternoon. There was a significant difference ($p<0.001$) between the groups in all dimensions of fatigue except the cognitive/mood dimension, which was also approaching significance. The most marked decline was seen in the behavioral/severity and affect domains. There was no significant difference in the scores between days or between weeks.

Conclusion: Compared to normal individuals, post-polio patients are significantly more fatigued, particularly in early afternoon. The RPFS was sufficiently sensitive and reliable that it may be useful in future therapeutic trials.

P-106

Learning a Simple Manual Task Using a Mirror

P. Chouinard, G. Leonard, T. Paus (Montreal, Quebec)

Background: It has been shown that therapy using a mirror can enhance post-stroke recovery in an affected upper limb (Altschuler et al., 1999). This study investigates the effectiveness of mirror training in healthy subjects.

Methods: Right-handed subjects (n=32) who had a left-hand superiority for a simple manual task participated in the study. Subjects practiced this task for 20 minutes on 5 consecutive days. Training consisted of observing movements of the left hand in a mirror, which then appears to be the right hand. The mirror was placed along the midline and between the hands. Group-1 moved both hands while Group-2 moved only the left. Two control groups that did not use the mirror were also included. Progress was documented daily and three days after training.

Results: Improvement in the less adept hand (right) was greater in the groups that moved both hands, whether or not they used the mirror ($F=5.32$, $p<0.05$). Mirror training did not improve performance of the right hand, and interestingly, tended to interfere with the ability of the left.

Conclusion: In healthy subjects, repetitive exercise enhances motor skill more than mirror training.

P-107

Familial Devic's Disease

M. Keegan, B. Weinshenker (Rochester, Minnesota, USA)

Background: Devic's disease is an uncommon idiopathic inflammatory demyelinating disease that exclusively involves the optic nerves and spinal cord. Most cases are sporadic. It remains controversial whether it is distinct from MS.

Methods: Case reports of two sisters with Devic's disease.

Results: The index case, one of 12 siblings of Spanish-

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American ancestry, developed a myelopathy in 1980 at age 26. The following year she developed simultaneous bilateral optic neuritis followed by numerous subsequent relapses resulting in almost complete bilateral blindness and spastic-ataxic gait. Her sister developed optic neuritis in 1993 at age 28. She experienced relapses of both inflammatory myelopathy and of optic neuritis involving both eyes. MRI scans of both patients showed longitudinally extensive inflammation and/or severe atrophy of the spinal cord highly consistent with Devic's. MRI of the brain in one sister was normal and was not performed in the other.

Conclusions: The occurrence of two cases of a relatively rare form of inflammatory demyelinating disease in a single pedigree would support Devic's being distinct from MS and that it may have a genetic basis in some families. The onset of symptoms at roughly the same age separated in time by 13 years suggests a genetic rather than environmental etiology.

P-108

Focal Cryptococcal Spinal Meningitis in an Immune Competent Host: A Case Report.

R.G. Kerr, R.J. Fox (Edmonton, Alberta)

A 53-year-old male who had immigrated to Canada from Trinidad 20 years ago presented with 3 weeks of non traumatic, intensifying lower back and right leg pain, as well as, progressive right leg weakness and some difficulty voiding over the last two weeks. The man had no constitutional symptoms and no other neurological or clinical findings. An MRI study of the lumbar spine revealed in addition to multilevel stenosis, extensive nodular intramedullary enhancement particularly at the L2, L3, and L4 levels, and enhancement of the nerve roots at these levels suggestive of leptomeningeal metastases. A metastatic work up provided normal hematology, normal abdominal and pelvic organs, an incidental dural based parasagittal intracranial lesion characteristic of a meningioma, and perihilar lymphadenopathy which following bronchoscopy and mediastinoscopy was diagnosed as inactive pulmonary sarcoidosis. CSF from a lumbar puncture was positive for cryptococcal infection. The patient is immune competent with no known infectious contacts or history of recent travel. A 10 week course of fluconazole was prescribed at the end of which there was marked improvement in ambulatory ability but a debilitating increase of pain symptoms. Follow-up cultures were negative for cryptococcus. Follow-up MR imaging indicated resolution of the nodular enhancement pattern but diffuse inflammatory changes consistent with arachnoiditis now pervade. Though cryptococcal meningitis is not rare, especially among the immune compromised, there are no other cases in the literature that describe a similar presentation of focal neurologic findings and isolated spinal cryptococcal meningitis without constitutional symptoms in an immune competent individual.

P-109

Clinical, Radiologic and Pathologic Correlates in Neuro-Behcet's Disease

S.M. Mirsattari, G.J. McGinn (Winnipeg, Manitoba), W.M. Halliday (Toronto, Ontario)

Background: Behcet's disease is a chronic relapsing multisystem inflammatory disorder of unknown etiology that frequently involves the central nervous system (CNS). Clinical, radiologic, and pathologic correlative studies of neuro-Behcet's disease are rare.

Patient and Method: Clinical, radiologic, and pathologic correlations in a case of neuro-Behcet's disease is reported.

Results: We are reporting a case of Behcet's disease with early and prominent neurological involvement. Clinically, she presented with a relapsing-remitting meningoencephalitis following an episode of streptococcal pharyngitis. Serial cranial magnetic resonance imaging studies revealed a progressive and severe focal atrophy restricted to the brainstem, midbrain, and cerebellum. Clinical relapses were associated with increased signal intensity in the brainstem and midbrain on the proton density and T2-weighted images. Ten years after the initial presentation, extensive autopsy revealed an active on chronic meningoencephalomyelitis involving all levels of the central nervous system (CNS) which was most marked in the brainstem and midbrain. There was marked atrophy of the brainstem and midbrain with mild to moderate atrophy elsewhere in the CNS. The pathology ranged from areas with hypercellularity associated with T-cells lymphocytic infiltrate, macrophages, parenchymal reactions to areas with tissue damage associated with axonal swelling, neuronal loss, gliosis, and perivascular lymphocytic cuffing with no luminal infiltration or thrombosis. There were minimal areas of softening and ischemia in the brain and moderate amount in the spinal cord. The arachnoid was fibrotic with patchy and scant lymphocytic infiltrate.

Conclusions: This case demonstrates that neuro-Behcet's is a diffuse disease of possible autoimmune origin which may be triggered by Streptococcal species and present with focal clinical and radiologic manifestations.

P-110

Spontaneous Intracranial Hypotension in the Absence of Magnetic Resonance Imaging Abnormalities

K. Schoffer, T.J. Benstead, I. Grant (Halifax, Nova Scotia)

Background: Spontaneous intracranial hypotension (SIH) is an uncommon clinical syndrome whose underlying cause is often obscure. The cardinal features of SIH are low cerebral spinal fluid (CSF) pressure, postural headache, and characteristic magnetic resonance imaging (MRI) findings.

Methods: Four symptomatic cases of SIH presented over a six month period. In each case, a diagnostic lumbar puncture (LP) and MRI study was performed.

Results: All four patients demonstrated CSF pleocytosis and protein elevation. None demonstrated growth in any CSF culture or positive cytology. Three of the patients exhibited MRI findings of diffuse spinal and cerebral epidural gadolinium

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enhancement and extradural fluid collections. One patient had no MRI abnormalities despite prominent postural headache and reduced CSF pressure at lumbar puncture. All patients recovered without surgery or blood patch.

Conclusions: MRI abnormalities are found in most, but not all patients, with SIH. CSF abnormalities can be detected even in patients with normal MRI. It is important to recognize the variable diagnostic results in this usually benign disorder.

P-111

Superficial Siderosis of the Central Nervous System: Case Report and Review of the Literature

C. Toth, A. Kirk (Saskatoon, Saskatchewan)

Background: Superficial siderosis is a rare cause of chronic cerebellar and brainstem dysfunction which often remains idiopathic.

Methods: We describe the clinical presentation and radiologic assessment of a 47-year-old Aboriginal male patient with a chronic four year history of gait and limb ataxia, spasticity and sensorineural deafness.

Results: Our patient presented with a four year history starting with sensorineural deafness, tinnitus to the right ear, and followed by ataxia of gait and limbs. Magnetic resonance imaging (MRI) of the brain showed diffuse hypointensity outlining the brainstem, cerebellum, cranial nerves VII and VIII bilaterally, and portions of the cerebral hemispheres as well as cerebellar atrophy. MRI of the spine demonstrated a cystic lesion compatible with a meningocele or pseudomeningocele at the T1/2 level as well as T10/11 disc protrusion causing significant cord compression. Clinical progression continued to worsen following discectomy. MRI and angiography of the cerebral vessels failed to show evidence of an arteriovenous malformation or aneurysm or other evidence of chronic subarachnoid leakage.

Conclusion: Superficial siderosis of the CNS is a rare cause of chronic cerebellar and brainstem dysfunction which remains idiopathic in almost 50% of patients. Most cases of superficial siderosis are thought to be due to chronic subarachnoid blood leakage and have identifiable causes in 54% of cases.

P-112

The Syndrome of Headache, Neurological Deficit, and Cerebrospinal Fluid Lymphocytosis (HaNDL): A Case Series of Eight Patients.

C. Toth, A. Kirk (Saskatoon, Saskatchewan)

Background: The syndrome of headache, neurological deficit, and cerebrospinal fluid (CSF) lymphocytosis (HaNDL) remains an uncommon, poorly understood process.

Methods: We describe the clinical presentations and CSF findings in eight cases of HaNDL syndrome. All cases had serial lumbar punctures performed to assess CSF changes over time.

Results: Eight patients presented with multiple episodes of focal neurological deficit associated with headache. There were five males and three females with a mean age of 28 years (range 18-50 years) at presentation. During the course of symptoms, there were a mean of 3.6 discrete episodes (range 2-6) of neurological deficit each associated with headache and followed by resolution. The length of symptomatic course was a mean of 15 days (S.D. = 7 days) with all patients returning to an asymptomatic state. CSF examination showed elevated opening pressure, lymphocytic pleocytosis, and elevated CSF protein in all cases. Each of these CSF parameters peaked in quantity during the illness before gradually returning to normal values with CSF abnormalities persisting long after symptoms had resolved in each case.

Conclusion: Patients with HaNDL syndrome have a transient course of neurological deficit associated with headache which recurs numerous times over the course of the illness before resolving. HaNDL is a self-limited syndrome with good outcome.

P-113

A Profile of Multiple Sclerosis (MS) Patients in Long-term Care Centres using the Continuing Care Needs Determination Instrument (CCNDI)

S. Warren, K.G. Warren, P. Beaulne, M. Lyle, C. Schalm, M. Wanke (Edmonton, Alberta), M. Hollander (Victoria, British Columbia)

Background: Very few descriptions of MS patients residing in long-term care centres have been published. Canadian long-term care centres have begun to collect standardized client assessments, which will establish a profile of these MS patients compared to other residents.

Methods: Recently Alberta Health and Wellness developed a new assessment tool, the CCNDI, which includes measures of activities of daily living (ADL), cognition, depression and behaviour problems. Items for this tool came from the Minimum Data Set: Version 2 and the Alberta Assessment and Placement Instrument (AAPI), which have been tested for reliability and validity. The sample consisted of 1,845 long-term care centre residents (15% of the total) province-wide.

Results: 96 (5%) of the residents sampled were diagnosed with MS. These individuals represented 25% of the chronically disabled service type client (49% of those ages 18 to 55). On basic demographic characteristics, MS patients were similar to all other residents on gender (69 to 68% female), but younger on current age (X=58 to 80 yrs). More MS patients scored severely impaired on physical ADL than other residents (72 to 24%), while fewer scored as having any instrumental ADL impairment (34 to 61%). Fewer MS patients were severely cognitively impaired than other residents (24 to 44%), gave indications of depression (48 to 61%) or behaviour problems (38 to 52%). MS patients required more minutes of care on average than other residents (X=196 to 159 min/day), according to a staff time use analysis.

Conclusion: Such information provided by databases can be useful in identifying the burden of disease due to various neurological conditions and their care requirements. MS patients account for a significant percentage of chronically disabled service type residents in Alberta long-term care centres, which may represent circumstances in Canada as a whole.

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NEUROPHYSIOLOGY

P-114

Use of the Collision Technique to Improve the Accuracy of Motor Unit Number Estimation

K. M. Chan, Y. Aoyagi, F. J. Strohschein (Edmonton, Alberta)

Background: Motor unit number estimate (MUNE) is a useful guide for measuring motoneuronal disease progression and for gauging the response to treatment. The multiple point stimulation method circumvents the problem of alteration and, in conjunction with force measurements, can provide a wide range of motor unit (MU) physiological information. However, a potential drawback is that if the same MUs obtained by stimulating the nerve at different points are inadvertently included, it can distort the size of the average motor unit action potential (MUAP) and hence the MUNE.

Methods: We used the collision technique to confirm whether two MUAPs with similar size and configuration obtained at different locations along the median nerve were generated by the same MU. Two normal subjects, one patient with carpal tunnel syndrome and one post-polio patient were studied.

Results: While the risk of stimulating the same MU at widely separate locations was negligible in normal subjects, this risk was much higher in patients with depleted motoneuron pool. The inadvertent inclusion of the same MUs, when not corrected, resulted in markedly reduced accuracy of the MUNE.

Conclusion: The collision technique can help to improve the accuracy of MUNE in patents with depleted motoneuron pool.

P-115

Artifact-free EEG Video Recording System (AFEEGRS) forAcute and Chronic Epilepsy Models in Rodents

M.A. Cortez, O.C. Snead III (Toronto, Ontario)

Background: There are no artifact-free EEG tools to approach the developmental epileptogenesis in chronic animal models.

Methods: EEG video recordings on AY9944 (AY) induced atypical absence epilepsy and add on proconvulsants to ascertain the coexistence of multiple seizure types in unrestrained behaving rodents (rat N= 20, mice N= 12). Subjects were implanted with 4 cortical monopolar and one scalp referential electrodes, linked to a head connector with FET preamplifiers and battery, signal conditioning device (5000x gain, 1Hz-100Hz filters, Axon Instruments), A/D converter (MP100 Biopac) and video/PC-PC video computer boards for recording image data.

Results: AFEEGRS recordings disclosed AY spike-and-wave discharges (SWD) with staring, vibrissal twitching and ability to move. AFEEGRS recordings of add on Pilocarpine or chemoconvulsant (bicuculline 5 mg/kg, Picrotoxin 37.5 mg/kg, pentylenetetrazole 37.5 mg/kg) treated subjects depicted bilateral forelimb clonus to generalized tonic clonic seizures, with generalized high amplitude spikes, spike clusters and postictal amplitude decrements, respectively. Seizure types coexisted with AY absences in rat and mice providing the sequence of convulsive and non convulsive EEG events.

Conclusions: AFEEGRS is a reliable tool for seizure type video EEG recording in chronic and/or acute epilepsy models and may be useful in chronic genetic epilepsy mice models.

P-116

The Utility of Neurophysiological Testing in Bell's Palsy: The Toronto Bell's Palsy Study

Michael D. Hill, (Calgary, Alberta) Gyl Midroni, Andrew M. Morris, Don E. Low (Toronto, Ontario)

Background: In the fall of 1997, an outbreak investigation was conducted into the possibility that an epidemic of Bell's palsy had arisen in the Greater Toronto area. A survey was conducted to identify patients with Bell's palsy. A sub-group of these patients were studied neurophysiologically. We were able to assess the utility of neurophysiological testing in Bell's palsy.

Methods: Patients with Bell's Palsy were asked if they would be willing to participate in more detailed neurophysiological testing. 44 patients were studied neurophysiologically. Neurophysiological assessment of the facial nerve included bilateral facial nerve conduction studies stimulating at the stylomastoid foramen and recording over the ipsilateral nasalis, bilateral blink responses and electromyography of the ipsilateral orbicularis oris, orbicularis oculi, nasalis and frontalis. Where indicated contralateral EMG was performed. Because of the nature of the study, patients underwent neurophysiological assessment at a variety of times after onset of their Bell's palsy.

Results: 224 patients were identified in the survey. Of these 44 agreed to undergo neurophysiological testing. No differences were observed between the two groups. 32 of 44 patients fulfilled clinical criteria for idiopathic facial palsy (Bell's palsy). 27(84%) of these patients had at least one neurophysiological abnormality. Electromyography was additionally helpful in only one patient in confirming seventh nerve dysfunction. Facial nerve conduction studies showed a high specificity (94%) but lower sensitivity (56%). Blink responses showed specificity (94%) and sensitivity (81%).

Conclusions: A major advantage of this study was its population based nature, avoiding referral bias seen in other studies. Blink responses showed the best sensitivity and specificity while electromyography was diagnostically useful in only one patient.

P-117

Performance Sensori-motrice de Sujets Contrôles et de Sujets Pariétolésés

M. Prud'Homme, J. Messier, T. Brochier, L. Sergio, J.F. Kalaska, N. Gosselin-Kessiby, A. Bouthillier (Montréal, Québec)

Documentation de base: Cette étude examine le rôle du cortex pariétal postérieur dans la planification et l'exécution de mouvements visuellement guidés. La planification de ces mouvements nécessite la transformation des informations sensorielles concernant la localisation de la cible et du bras en une séquence de variations d'angles articulaires appropriées au déplacement de la main vers la cible. Des études

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psychophysiques ont suggéré que les imprécisions motrices des sujets pariétolésés s'expliquent par des déficits dans les transformations sensori-motrices qui précèdent l'initiation des mouvements sans atteinte de la coordination motrice. Cependant, d'autres études ont rapporté des déficits importants dans la coordination interarticulaire de mouvements complexes. Cette discordance pourrait être expliquée par le fait qu'aucune étude n'a combiné l'évaluation de la précision des mouvements à celle de la coordination interarticulaire.

Méthodes: Un système d'analyse de mouvements (Optotrack) nous a permis d'examiner les performances perceptives et motrices de sujets contrôles et pariétolésés lors de tâches qui requièrent différentes transformations sensori-motrices et différentes coordinations interarticulaires.

Résultats et conclusions: Chez les sujets contrôles, la nature des transformations sensori-motrices a produit un effet significatif sur la précision des mouvements. La comparaison entre la performance motrice des sujets contrôles et des sujets pariétolésés pour ces différentes conditions expérimentales permet de distinguer les imprécisions motrices attribuables à des déficits dans les transformations sensori-motrices de celles attribuables à des déficits dans la coordination interarticulaire.

P-118

Rippling Muscle Disease: Analysis of a Large Mauritian Kindred

Daniel Wong, Pierre R. Bourque (Ottawa, Ontario), Dietrich A. Stephan (Bethesda, M.D.)

Background: Rippling muscle disease is a rare disorder characterized by electrically silent muscle mounding and rippling. It has been described in sporadic and autosomal dominant forms, the latter linked to chromosome 1q41 by positional cloning.

Methods : A large Asian kinship was studied, with members in Canada and on the Island of Mauritius. Clinical assessment consisted of a standardized questionnaire and motor examination, including tests for percussion-induced mounding and rippling. Blood samples were drawn, with a genetic strategy focussed on first testing for locus 1q41, then other ryanodine loci (Chr 15 & 19). Muscle biopsy and EMG were done on the proband.

Results : Electromyography confirmed the electrically silent nature of muscle mounding. Muscle biopsy findings, both at light and electron microscopy, were non-specific. Twenty-two affected individuals were identified. Muscle cramping with non-strenuous exercise was the most frequent symptom. Percussion-induced mounding was best elicited on the biceps brachii. True rippling was rarely found.

Conclusions: Rippling muscle disease may be clinically heterogenous, presenting with largely asymptomatic percussion-induced focal muscle mounding. Its genetic delineation may shed light on processes involved in muscle fiber excitation/contraction coupling. Genetic studies are under way in this very large kinship, starting with Chr 1q41 and other ryanodine-associated loci.

P-119

Quantified Electroencephalography: Differences Between Eyes Closed and Eyes Open

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Background: Comparison of eyes closed (EC) and eyes open (EO) spectral topographies in healthy subjects may prove helpful in electroencephalographic (EEG) interpretation.

Methods: Subjects: Seventy healthy volunteers (age: 17-73 years; M/F: 36/34). Data collection: Twenty channels of 10/20 configured referential (linked ears) data were acquired in six frequency bands in the alert condition. Analyses: Each electrode was assigned Cartesian coordinates so that the response surface could be described as a bivariate polynomial in x and y. Transformations of this equation yielded univariate polynomials describing coronal and sagittal sections. Bootstrap multivariate statistics were used to compare the equations.

Results: Spatial features differed between conditions in all frequency bands ($p<.0001$). There was localized fronto-temporal increase in EC delta and in both frontal and occipital alpha. A fronto-temporal EO beta power pattern tended to differ from a more posterior EC pattern. Increased EC total power declined the more distant the frequency band was from alpha.

Conclusions: (a) Residual eye movement artifact may account for the delta observations. (b) The distribution of superior EC power in alpha may reflect the location of alpha generators which show considerable frontal activity. (c) Differences in the distribution of muscle related spectral intrusions in EC and EO may account for the beta band observations.

MOVEMENT DISORDERS

P-120

Deep Brain Stimulation in the Management of Hemidystonia

S.D. Christie, D. King, I. Mendez (Halifax, Nova Scotia)

Background: Dystonias, syndromes of sustained abnormal postures, often result in impairment of movements as a result of alteration in muscle tone. Treatments involve a variety of medications including anticholinergics, dopamine depleting agents, anti-spasmotics and membrane stabilizing drugs. Injections of botulinum A toxin is used for severe focal dystonias. Surgical management has been largely reserved for severe cases not responding to medical intervention. Approaches include intra- and extradural denervation procedures, spinal cord stimulation and pallidotomy. Herein we present a case of hemidystonia treated successfully with continuous pallidal stimulation.

Methods: A review of the literature and report of clinical case.

Results: A 45 year-old man was referred to our service after an 11-year history of right-sided hemidystonia. Initial management involved multiple medications, including botulinum A toxin injections. His clinical course was

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progressive, painful and he was having difficulty performing in the workplace. Pre- and post-operative evaluations included MRI imaging, physical examination and assessment using the Fahn-Marsden Evaluation Scale. Under neurolept anaesthesia a permanent Medtronic deep brain stimulator was stereotactically placed in his left ventral posterolateral pallidum. There was complete resolution of his dystonic symptoms when the stimulator was turned on. The beneficial effect of stimulation has been sustained for 9 months.

Conclusions: Deep brain pallidal stimulation may be considered as a treatment option in the management of patients with progressive, disabling dystonia which are not satisfactorily controlled with medications.

P-121

Reversible Parkinsonism, Sudden Stupor, and Hyperammonemia in a Patient with Portal Vein Thrombosis

P. Federico, D.W. Zochodne (Calgary, Alberta)

Background: Portal-systemic encephalopathy is often associated with hyperammonemia that complicates chronic hepatic disease.

Methods: We report an unusual case of reversible parkinsonism followed by sudden stupor in a patient with unrecognized hyperammonemia and portal vein thrombosis.

Results: An active 90-year-old male developed slowing, poor 'momentum', and resting hand tremor over six months. Examination showed asterixis, bradykinesia, cogwheel rigidity in all limbs, bilateral rest tremor, and a parkinsonian gait. Serum venous ammonia was 145 μM (normal 12-47 μM). The next day, the patient became unresponsive with eye opening and limb withdrawal to pain only. Serum ammonia was now 178 μM. Lactulose therapy was started and within 1 week, the serum ammonia level normalized and examination showed only minimal parkinsonism. An abdominal CT identified portal vein thrombosis with porto-systemic shunting that reversed after 7 months of treatment. Examination after two years showed no signs of parkinsonism.

Conclusions: Parkinsonism can dominate the early clinical picture of patients with hyperammonemia before the onset of portal-systemic encephalopathy. The underlying mechanism(s) are unclear but likely relate to disruption of neurotransmission in the basal ganglia.

P-122

Pharmacoeconomic Analysis of Ropinirole (ReQuip®) versus Levodopa + Benserazide (Prolopa®) in the Treatment of Parkinson's Disease

M. Iskedjian, N.A. Kulin (Hamilton, Ontario), T.R. Einarson (Toronto, Ontario)

Background: We examined the economic impact of the reducing dyskinesias by using Requip® [ropinirole (R)] instead of Prolopa® [levodopa+benserazide (LDB)], in Parkinson's Disease.

Methods: A model was developed to represent direct healthcare costs (medications, physician visits, hospitalizations, long-term care), productivity loss and caregiver time over 5 years. Dyskinesia rates were derived from a 5-year double-blind RCT. Resource utilization was based on the literature and expert opinion. The analysis was performed from the Ontario Ministry of Health (OMH) and societal perspective, using standard costs. Sensitivity analyses were performed on the rates of dyskinesias and caregiver time.

Results: The intent-to-treat analysis, based on disabling dyskinesia rates of 8% for R and 22% for LDB, produced daily overall costs/patient of $9.38 for R and $11.21 for LDB, resulting in overall daily savings of $1.83/ patient for R ($1.61, discounted at 3%). Healthcare costs with R were $4.41/patient/day more than LDB ($4.58 for medications), but treatment with R saved $4.37 daily in avoided productivity loss and $1.87 in caregiver time.

Conclusions: Ropinirole reduces the need for rescue LDB and dyskinesia rates. From a societal perspective, it produces additional savings offsetting its higher acquisition cost, and making it a cost-effective alternative when compared to levodopa+benserazide.

P-123

Enhancement of Sensorimotor Behavioural Recovery in Hemiparkinsonian Rats with Intrastriatal, Intranigral, and Intrasubthalamic Nucleus Dopaminergic Transplants

K. Mukhida, D. Sadi, K.A. Baker, I. Mendez (Halifax, Nova Scotia)

Background: The subthalamic nucleus (STN) has a central role in basal ganglia physiology and PD symptomatology. Inactivation of the STN can improve akinesia, tremor, and rigidity in PD. The aim of this project was to determine if the STN is an important target for neural transplantation by assessing whether intrasubthalamic nucleus grafts can restore complex sensorimotor behaviours in the Parkinson rat model.

Methods: Female Wistar rats made hemiparkinsonian with 6-hydroxydopamine were randomly assigned to one of eight groups: one group received lesions only and others were transplanted with 900 000 embryonic day 14 rat ventral mesencephalic cells in the i) substantia nigra (SN), ii) striatum (ST), iii) STN, iv) ST and SN, v) ST, SN, and STN, vi) SN and STN, and vii) ST and STN. Behaviours were assessed using the amphetamine challenge, staircase, and stepping tests. The animals were sacrificed nine weeks post-transplantation and grafted cell survival was analyzed using tyrosine hydroxylase immunohistochemistry.

Results: Animals that received simultaneous intrastriatal, intranigral, and intrasubthalamic grafts demonstrated histologic reconstruction of the nigrostriatal dopaminergic pathway and significant improvement in functional recovery compared to animals that received these grafts alone. Rotational behaviour improved in animals with striatal transplants and forelimb function improved in animals with nigral and/or subthalamic transplants. Simultaneous transplants in the three structures significantly attenuated the motivational component of akinesia.

Conclusions: These results suggest that restoration of

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dopaminergic activity to the ST, SN, and STN through neural transplants restores sensorimotor behaviours and reconstructs the nigrostriatal dopaminergic pathway in the hemiparkinsonian rat, and suggest that the STN can be considered a potential target for clinical neural transplantation strategies for PD.

P-124

A Quantitative Study of Cell Death of Nigral Neurons in Rat Model of Parkinson's Disease

J.Y. Park (Seoul, Korea), S. Kalia, L. Liu, A. Lozano (Toronto, Ontario)

Background: The purpose of this study was first to make a rat model of Parkinson's disease by complete transection of nigrostriatal pathway to investigate the degree and time course of retrograde neuronal death in substantia nigra pars compacta (SNpc). The second aim was to identify which subpopulation of these dopaminergic neurons may be more vulnerable or resistant to axotomy. Also, a preliminary study was conducted to observe whether a peripheral nerve graft implanted close to the transection could rescue these neurons.

Methods: A retrograde tracer, DiI, was injected into striatum of both sides 7 days prior to the transection. A modified technique involving transection of medial forebrain bundle (MFB) at 1 mm rostral to tip of SN with a custom-designed wire knife was used. Animals were assigned to each time interval group (~16 weeks). Degree and location of cell death, and counting of survived neurons was done by tyrosine hydroxylase (TH)-immunohistochemistry, and computer image software (SigmaScan) was used for measurement and mapping.

Results: DiI labelled SNpc neurons represented over 90% of TH(+) neurons in all groups including normal groups. Death of nigral neurons progressed over several weeks, but after 4 weeks, only 5.1%-7.0% of neurons remained when compared to the intact side. However, by double labeling, it was demonstrated that these remaining neurons most likely have contralateral projections. The size of the neurons also decreased significantly. Surviving neurons were located mostly within the medial half of SN close to ventral tegmental area (VTA). Completeness of lesion was correlated with the absence of TH-immunoreactivity in the striatum. When a tibial nerve is implanted (autograft, n=8) into MFB after its transection and examined after 16 weeks, there was a substantial number of surviving nigral neurons (~ 35%).

Conclusions: With this modified technique, a complete cell death in SNpc is seen by 4 weeks after transection of MFB. Neurons in the medial region survived longer than those in lateral group. A substantial regeneration of SN neurons after peripheral nerve graft implantation indicates that it should be possible to implant a graft between the SN or MFB and denervated striatum in order to determine whether dopaminergic reinnervation and functional improvement occurs.

PERIPHERAL NERVE SURGERY

P-125

Brachial Plexus Tumors: Case Presentations

Line Jacques (Montreal, Quebec)

Background: Brachial plexus tumors are rare clinical entities, usually consisting of benign lesions such as schwannomas or neurofibromas. Surgical extirpation is considered therapy of choice, although neurological deficits may arise from such intervention. Other complications, such as vascular or pulmonary injury, are possible.

Case Presentations: We present 12 operatively treated brachial plexus tumors, including cases of schwannoma, neurofibroma, leiomyosarcoma, and chondrosarcoma, with an additional lesion of unclear pathologic composition. Differential diagnosis of brachial plexus tumors is reviewed.

Results: Surgical resection was accomplished in each case, without development of new neurological deficit. Associated perioperative complications were minimal.

Conclusion: Surgical treatment of brachial plexus tumors may be accomplished with minimal morbidity. Although the most frequent lesions consist of benign nerve sheath tumors, other pathologic processes should be considered in the differential diagnosis of these unusual patients.

P-126

Surgical Management of Lumbarsacral Plexopathy.

Line Jacques, Chantale Desbiens, Jacob Garzon, Nathan Sheiner, Issie Weisglass, (Montreal, Quebec)

Background: Lumbarsacral plexopathy is a rare clinical entity. It may arise secondary to compression such as hematoma, infiltration by neoplastic process or by trauma.

Methods: 4 cases of lumbarsacral plexopathy will be presented: a presacral S1 root schwannoma, T12-L1 malignant neurofibroma, lumbarsacral stab wound and a hematoma yielding compression. Differential diagnosis will be reviewed.

Results: Intraoperative nerve action potential was used in all cases. A retroperitoneal approach was performed by a general or a cardiovascular surgeon. Surgical resections of the tumour were accomplished in each case without development of new neurological deficit. Associated perioperative complications were minimal.

Conclusion: Although benign nerve sheath tumours are the most frequent neoplasms, malignant processes can occur. Traumatic lumbarsacral plexopathy is very unusual : in this case, an excellent result was obtained following operative treatment. Surgical management of lumbarsacral plexopathy may be accomplish with minimal morbidity.

P-127

Surgical Resection of Paraspinal Nerve Sheath Tumors with the Assistance of Endoscopic Ultrasonic Aspirator

K. Reddy, N. Murty, J. Miller (Hamilton, Ontario)

Background: Paraspinal nerve sheath tumors have been

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traditionally treated by open surgery. With the development of endoscopic spinal surgery, there have been sporadic case reports of endoscopic surgery for these lesions.

Methods: The authors wish to present two cases of paraspinal benign nerve sheath tumors that were resected thoracoscopically using an ultrasonic aspirator.

Results: Case #1: A 67-year-old male with known carcinoma of the prostate, incidentally discovered to have a large dumbbell tumor at T9-10 on the right side. Other than mild localized discomfort he had no symptoms related to this lesion. An endoscopic resection was undertaken using an ultrasonic aspirator. We were able to achieve a gross total resection with satisfactory post operative outcome.

Case #2: A 22-year-old right handed male with pain in the upper thoracic paraspinal region. Investigations in the form of a CT scan and MRI revealed a left paraspinal (likely sympathetic chain related T2 neoplasm). This lesion was endoscopically resected (subtotally because of attachments to great vessels). A post operative pneumothorax was treated with good eventual outcome. These cases demonstrate that endoscopic resection of benign nerve sheath tumors is entirely possible and safe and can be performed with the assistance of an ultrasonic aspirator.

Conclusion: The authors feel in fact that this approach should be given consideration as first line therapy for paraspinal benign nerve sheath tumors in appropriate cases.

P-128

Radiation Induced Peripheral Nerve Tumors

G. Zadeh, P. Shannon, M. Bance, S. Wong, A. Guha (Toronto, Ontario)

Background: Tumors of the peripheral nerves, both malignant and benign, are rare reported complications of radiation therapy.

Methods/Results: We present the case of a thirty-year-old male without Neurofibromatosis1 (NF1), who presented with an enlarging neurofibroma of the brachial plexus, arising twenty years after radiation therapy to the region for Hodgkin's Lymphoma. The pathology demonstrated a moderate degree of nuclear atypia, hypercellularity, and a high proliferative index suggestive of pre-malignant transformation. Two other cases of such atypical neurofibromas have come to our recent attention, all arising in non-NF1 patients who have been radiated many years previously, and these will also be discussed.

Conclusions: There are only three other reports of post-radiation neurofibromas in the literature. These cases and our own demonstrate features of aggressive growth compared to sporadic or NF1 associated neurofibromas. Focused radiation is being increasingly advocated as primary treatment of benign vestibular schwannomas, even in young patients and those with germline pre-disposition syndromes such as NF2. These cases illustrate that radiation can be a potential carcinogen to peripheral nerves, a well recognized longterm complication after radiation to the central nervous system. It is our belief that our exponential clinical experience in the use of focused radiation in nervous system tumors, should be matched by increased molecular understanding of its radiobiological consequences.

PAIN

P-129

Role of Intrathecal Morphine in Control of Chronic Benign Pain

Michael Kelly (Saskatoon, Saskatchewan), Krishna Kumar (Regina, Saskatchewan)

Background: We present long-term effects of continuous intrathecal morphine infusion therapy in 16 patients with chronic, nonmalignant pain syndromes.

Method: In the last five years, 16 patients received fully programmable Synchromed pumps for intrathecal drug delivery. The drugs used were morphine or morphine in combination with clonidine. The follow-up period ranged from 13 to 49 months (mean 29.14 months).

Results: 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 long-term observation, no patient had a constant dosage history. The patients who received intrathecal morphine for longer than 2 years all showed an increase in morphine dosage to more than 10 mg/day. The best long-term results were seen with deafferentation pain and mixed pain, with 75% and 61% pain reduction (visual analog scale), respectively. Nociceptive pain patients had best pain relief initially (78% pain reduction) but tended to decrease over the follow-up period to a 57% pain reduction at final follow-up. The average pain reduction for all groups after 6 months was 67.5% and at last follow-up, it was 57.5%. Ten patients were satisfied with the delivery system and eleven reported improvement in their quality of life. Four patients were considered failures, in two morphine alone or in combination produced poor pain control and in the other two the side effects were intolerable and the pump had to be explanted. The complications consisted of one mechanical pump failure and one disconnection of the intrathecal catheter. The side effects observed were constipation, disturbed micturition, pruritus, cold sweats and amenorrhea which improve with time.

Conclusion: Intrathecal opioids for nonmalignant pain is justified in carefully selected patients.

P-130

Chronic Neuropathic Pain: Long-term Results

C.P.N. Watson, J. Watt-Watson (Toronto Ontario)

The treatment of neuropathic pain is of increasing interest as new therapies emerge. Chronic opioid therapy is an important option. Long-term studies are essential to determine if this approach is safe and effective. This poster describes follow-up data of up to 25-years for these patients.

Method: Pain management was retrospectively examined for 80 patients seen every 2-3 months by a neurologist. Data were collected at each visit to describe pain intensity (0-10 scale), pain quality, treatment side effects, patients' satisfaction, and drug type and dose.

Results: Data were taken from files of 35 women and 45 men, with a mean age of 45-years, and diagnosed mainly with

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neuropathic pain. Pain relief was usually incomplete. Major issues to be discussed are chemical dependency, tolerance, physical dependency, suicide, psychiatric illness, type and dose of opioids, and side effects. Involvement of the regulatory body, the College of Physicians and Surgeons will also be discussed.

Conclusions: The treatment of non-malignant pain is a specialized area requiring a broad and in-depth knowledge. Patients must be selected carefully for treatment, especially for chronic opioid therapy, and be closely followed using reasonable guidelines. Major problems can arise in the course of such a practice.

P-131

Trigeminal Postherpetic Neuralgia Postmortem: Clinically Unilateral, Pathologically Bilateral: A Case Report and Review

C.P.N. Watson, R. Midha, S. Nag, C. Munro, J. Dostrovky, (Toronto, Ontario) M. Devor (Jerusalem, Israel)

An autopsy examination of postherpetic neuralgia (PHN) of the ophthalmic division of the trigeminal nerve is described. No comparable cases have been identified.

Method: The literature, with regard to postmortem studies of herpes zoster (HZ) ophthalmicus, was reviewed. Most of these studies were of acute zoster patients or those who did not clearly suffer PHN. They did, however, demonstrate pathology in the gasserian ganglion, in the peripheral nerve, and centrally. At autopsy, samples were collected from the affected and unaffected V nerve and ganglion, and the brain and brainstem were removed. These structures were examined by light and electron microscopy.

Results: This case was striking because of the presence of severe involvement of the ophthalmic nerve and the absence of any signs of change from the gasserian ganglion through to the thalamus. Contralateral peripheral changes were observed.

Conclusions: These findings are at variance with the data regarding spinal cases of PHN and from other cases of ophthalmic HZ because of the lack of central abnormalities. Peripherally there was a loss of large (?inhibitory) fibers and an excess number of small (?excitatory) fibers in the ophthalmic nerve both ipsilaterally and contralaterally.

P-132

Chronic Pain Treatment by Intrathecal Drug Administration: a Good Therapeutic Option for Failed Back Surgery Syndrome (FBSS)

Line Jacques, Emile Berger, Chantale Desbiens, Tina Del Duca (Montreal, Quebec)

Background: Patients with FBSS are very difficult to treat. Such patients have had already at least three operations, such as laminectomy, discectomy and/or fusion, without experiencing pain relief or achieving an acceptable functional level.

Methods: A multidisciplinary team has evaluated prospectively twelve (12) patients and six (6) underwent a trial phase for neuromodulation therapy that failed. After a successful intrathecal trial therapy, a pump for drug delivery was implanted.Results were evaluated by using the Oswestry and SF-36 questionnaires, a review of hospital charts, as well as clinical examination.

Results: Post-operatively, the frequency of visits to the emergency room decreased significantly and the quality of life was found to have improved without any increase in drug dosage.

Conclusion: Good selection of those patients within a multidisciplinary team is mandatory. The intrathecal drug delivery is a good therapeutic option for the patient's quality of life and decreases costs in the health care system.

BASIC NEUROSCIENCE

P-133

A Potential Role for Heme Oxygenase-1 in the Pathogenesis of Multiple Sclerosis

D.J. Sahlas, K. Mehindate, H.M. Schipper (Montreal, Quebec)

Background: Proinflammatory cytokines, iron deposition, and oxidative stress are implicated in multiple sclerosis (MS) lesion formation. We have previously shown interleukin-1β (IL-1β) and tumor necrosis factor-α (TNFα) upregulate the stress protein, heme oxygenase-1 (HO-1), promoting sequestration of ^{55}iron by rat astroglial mitochondria.

Methods: Spinal cord tissue from 10 MS patients and three control subjects was immunohistochemically stained for the astrocyte-specific marker, glial fibrillary acidic protein (GFAP), and HO-1. Neonatal rat astroglial cultures were exposed to IL-1β or TNFα alone, or in combination with interferon β1b (INFβ). HO-1 mRNA levels were assessed by Northern analysis, and mitochondrial uptake of $^{55}FeCl_3$-derived iron determined by subcellular fractionation and scintillation quantification.

Results: The percentage of GFAP-positive astrocytes co-expressing HO-1 in affected spinal cord from MS patients (57.3% +/- 12.8% S.D.) was greater than in normal spinal cord from controls (15.4% +/- 8.4% S.D., p=0.0003). INF suppressed induction of the HO-1 gene, and blocked incorporation of mitochondrial iron in IL-1β- or TNFα-challenged rat astroglia.

Conclusions: HO-1 is over-expressed in MS spinal cord astroglia, and may contribute to the pathological deposition of redox-active iron in MS lesions. IFNβ may benefit patients with MS partly by attenuating HO-1 gene induction, and subsequent mitochondrial iron deposition, in astrocytes exposed to proinflammatory cytokines.

P-134

Role of Heme Oxygenase-1 in the Formation of Corpora Amylacea

D.J. Sahlas, A. Liberman, H.M. Schipper (Montreal, Quebec)

Background: Corpora amylacea (CA) are glycoproteinaceous inclusions accumulating in the human brain during normal aging, and to a greater extent in Alzheimer's disease. In cultured rat

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astroglia, cysteamine (CSH) upregulates heme oxygenase-1 (HO-1), with long-term exposure promoting formation of CA-like inclusions.

Methods: Primary cultures of neonatal rat astroglia were exposed to 880 μM CSH for three months, in the presence or absence of dexamethasone, a suppressor of HO-1 gene transcription. Cells were double-labeled with periodic acid-Schiff reagent (PAS) and antisera against ubiquitin or HO-1. CA were quantified and their immunofluorescent properties analyzed using confocal microscopy.

Results: HO-1 immunofluorescence was observed in 50-100% of CSH-exposed cells, compared to 25-50% of cells co-treated with dexamethasone. CA appeared as large (10-30 μm), spherical, intensely PAS-positive inclusions with rim-staining for ubiquitin and HO-1. Monolayers exposed to CSH alone exhibited more CA (5.6 +/- 4.0 S.D. / cm^2) than CSH-exposed cells treated with dexamethasone (50μg/ml: 2.4 +/- 2.2 S.D., 100μg/ml: 2.4 +/- 1.6 S.D.), or untreated controls (0.9 +/- 0.9 S.D. / cm^2, p=0.015).

Conclusions: As previously shown in human brain, CAin rat astroglia exhibit ubiquitin and HO-1 immunoreactivity. Dexamethasone reduces HO-1 immunofluorescence and suppresses CA formation in CSH-treated astroglia, supporting a role for HO-1 in their biogenesis.

P-135

Role of Apoptosis in Neuronal and Axonal Degeneration in Cervical Spondylitic Myelopathy: An Immunohistochemical Study of Human Autopsy Cases

M.G. Fehlings, W.R. Yu, P. Shannon, L.H.S. Sekhon (Toronto, Ontario)

Background: Although cervical spondylitic myelopathy (CSM) is the leading cause of spinal cord dysfunction, in older patients, little is known regarding the molecular mechanisms of neuronal and axonal degeneration. Apoptosis, or genetically programmed cell death, has been shown to contribute to the pathophysiology of neural ischemia and trauma. Given that compression and ischemia are two key mechanisms contributing to CSM, we investigated the role of apoptosis in this disorder.

Methods: Paraffin embedded sections of post-mortem cervical cord tissue from 8 patients with documented CSM (6M, 2F; mean age 69, range 61-89) and 4 control spinal cords (3F, 1M; mean age 51, range 43-61) were stained with hematoxylin-eosin/luxol fast blue and examined immunohistochemically for apoptosis by the TUNEL technique. Double labeling with cell specific markers (GFAP, MAP2, NF200, myelin basic protein and CD68) was undertaken to identify astrocytes, neurons, axons, oligodendrocytes and microglia respectively.

Results: Light microscopic analysis revealed prominent anterior horn cell loss, dorsal root degeneration and extensive loss of myelinated axons particularly in the dorsal and lateral columns. Furthermore, numerous TUNEL-positive oligodendrocytes (x=90.9±32.4) were present in white matter tracts in association with degenerating axons.

Conclusions: This is the first study to demonstrate that apoptosis of neurons and oligodendrocytes occurs in humans in CSM. Early surgical intervention, neuroprotective approaches, or gene therapy may attenuate this form of genetically programmed cell death.

P-136

Dysregulation of Metalloproteinases Expression in the Central Nervous System Vascular Malformations

D. Shedid, M.W. Bojanowski, J.L. Caron, R. Beliveau (Montreal, Quebec)

Background: Little is known about the pathogenesis of arteriovenous malformations (AVM) and about the mechanisms regulating the genesis and progression of intracranial aneurysms. Previous studies have suggested the possible role of metalloproteinases (MMPs) in the formation and rupture of intracranial aneurysms. MMPs are key enzymes involved in the formation of blood vessels and in extracellular matrix (ECM) remodeling. The purpose of this study is to assess the possible role of MMPs and their inhibitors in the pathogenesis of vascular malformations.

Methods: Specimens from 11 patients operated for intracranial vascular lesions (8 AVM and 3 aneurysms) and 3 controls were analysed. The expression of tissue inhibitor of metalloproteinases (TIMP-1) was determined by Western blotting. MMP activity was detected by gelatin zymography.

Results: The activity of MMP-2 was decreased in all of the AVMs and intracerebral aneurysms. There was higher expression of pro-MMP9. TIMP-1, an MMP9 inhibitor, was overexpressed in 6 of the 8 AVMs and all the aneurysms.

Conclusions: The imbalance of protease-antiprotease homeostasis reflected by TIMP-1 and pro-MMP9 over-expression, combined with an underexpression of MMP2 might suggest their involvement in the pathogenesis of AVMs and intracranial aneurysms. Thus, the abnormal vascular cell phenotype seen in these anomalies might be due to an ECM remodeling caused by the MMPs.

P-137

Retrograde and Anterograde Labeling of Spinal Cord Tracts in the Same Animal

E. Tsai, C. Tator (Toronto, Ontario)

Background: Anterograde and retrograde labeling of spinal cord tracts have traditionally been done in different animals. However, with this method spinal cord repair strategies have often produced disparate results in animals subjected to the same repair strategy. Such experiments may not allow accurate and complete study of the repair strategy. Therefore, we developed a method of labeling spinal cord tracts in both anterograde and retrograde directions in the same animal.

Methods: DiI, a lipophilic dye, was applied unilaterally to the sensorimotor cortex and gelfoam soaked in Fluoro-Gold (FG) was placed in the spinal cord at T13/L1 of adult rats. Other tracer combinations using DiI with DiA, DiO, Rhodamine Green dextran, or fluoroscein dextran were also investigated.

Results: With this method, in the same animal, DiI labeled the corticospinal tract, and FG labeled the cortical and brainstem nuclei of several spinal cord tracts. Control animals with

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complete spinal cord transection did not demonstrate diffusion of the tracers across the transection site.

Conclusions: Thus DiI and FG allow simultaneous anterograde and retrograde labeling of spinal cord tracts which should be useful for studies of spinal cord regeneration.

P-138

Intravenous Administration of a Novel Free Radical Trapping Agent Reduces Cortical Infarction After Permanent Focal Ischemia in Rats

Z.H. Zhao M.S. Cheng, A.M. Buchan, (Calgary, Alberta) K.R. Maples (San Francisco, California)

Introduction: Free radicals have gained wide acceptance as mediators of cerebral ischemic injury. It has previously been reported that a nitrone trapping agent, α-phenyl-N-tert-butyl nitrone (PBN), can reduce infarct volumes in rats subjected to both permanent or transient focal cerebral ischemia. A recent study has demonstrated that NXY-059, a novel free radical trapping compound, has a neuroprotective effect against transient focal cerebral ischemia. This study was designed to determine the effect of NXY-059 in a rodent permanent focal cerebral ischemic model.

Methods: Male spontaneously hypertensive rats were subjected to permanent middle cerebral artery occlusion (MCAO) using microclip. NXY-059, dissolved in saline, was given IV bolus within 5 minutes following MCAO and continuously infused for 24 hours at 30mg/kg (group 2) or 60mg/kg (group 3). The animals from group 1 were given saline as control. Infarction was quantified after a survival period of 24 hours and expressed in percentage. Differences in infarct volume were examined with one-way ANOVA following Dunnet's Multiple Comparison test.

Results:

Groups	% of Cortical Infarction	
1 (n=10)	22.6% ± 6.8%	
2 (n=9)	17.4% ± 6.8%	
3 (n=12)	14.5% ± 5.0%	* P=0.009

Conclusion: Our preliminary data demonstrate that 60mg/kg of NXY-059 ameliorates cortical infarction in rats subjected to permanent focal cerebral ischemia.

P-139

The Mitogenic Effects of Epidermal Growth Factor and Fibroblast Growth Factor 2 on the Neural Precursor Cells in the Ependyma of the Adult Rat Spinal Cord *in Vivo*

A. Kojima, C.H. Tator (Toronto, Ontario)

Background: Epidermal growth factor (EGF) and fibroblast growth factor 2 (FGF2) have a mitogenic effect on the neural precursor cells of the adult mammalian forebrain *in vivo*. We investigated whether these mitogens have similar effects on the neural precursor cells in the ependyma of the adult rat spinal cord *in vivo*.

Method: EGF, FGF2, EGF plus FGF2, or artificial cerebrospinal fluid (aCSF) was infused into the intrathecal space at T1 of the adult rat with an osmotic minipump for 3 or 14 days. The proliferative effect was evaluated with the bromodeoxyuridine (BrdU) labeling index (LI).

Results: At 3 days, there was no statistical difference in LI between these groups, but at 14 days, the LI was significantly higher in the EGF plus FGF2 group (27.2±16.0 %) than in the aCSF group (6.4±4.4 %) ($p<0.05$). With EGF alone or FGF2 alone, the LI increases were not significantly different from the aCSF group. With EGF plus FGF2 for 14 days, nestin immunoreactivity was shown in some BrdU positive ependymal cells.

Conclusion: Intrathecal infusion of EGF plus FGF2 for 14 days has a mitogenic effect on the neural precursor cells in the ependyma of the adult rat spinal cord *in vivo*.

TRAUMA

P-140

A Process Evaluation of the Think First For Kids Program in Canadian Schools

A. Sharman, M.D. Cusimano, E. Sam (Toronto, Ontario)

Background: Injuries are the leading cause of death of Canadian youth. By way of a multifaceted program with a school-based educational program at its core, the Think First for Kids Program (TFFK) aims to prevent such injuries. The purpose of this study was to evaluate the quality of the program and barriers to implementation from the perspective of teachers.

Methods: A survey of teachers was performed in 1998 and 1999. Questionnaire responses were analyzed quantitatively in terms of frequency distribution and qualitatively by open coding. Focus groups with teachers, school board officials and public health professionals were also held.

Results: 109 schools responded to the survey. Of the schools that responded and received the program (n=97), 75% implemented it in some form and 81% rated it as very good to excellent. Common themes included positive comments on the program's functional attributes, versatility and its "peer-to peer" approach.

Conclusion: It is evident that the TFFK program was widely embraced and highly regarded by school teachers. It became apparent that effective delivery of the program must be associated with contact and issued in a timely manner to facilitate curriculum integration. Overall, the teachers viewed the THINK FIRST FOR KIDS program as a valuable tool in teaching children important brain and spinal cord safety behaviours.

P-141

Curricular Mapping of the Think First for Kids Program to Ontario's new Primary Curriculum

A. Sharman, M.D. Cusimano (Toronto, Ontario)

Background: Injuries to Canadian youth are the most unrecognized public health issue facing Canadians. The Think First for Kids Program (TFFK) aims to prevent such injuries by means of a multifaceted school-based educational program. The province of Ontario and other provinces have mandated new

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curricular guidelines for children aimed at instilling healthy behaviours in children. Teachers need educational resources like TFFK to achieve mandated educational reforms. The purpose of this study was to evaluate the TFFK program for its ability to cover the required components of the new Ontario Curriculum (OC).

Methods: A detailed comparative analysis of TFFK and the OC was performed by two reviewers. With respect to different subjects, areas of significant overlap were recorded by OC subject area, TFFK content area, and the OC page number. A "Mapping" of the TFFK to the new OC was thus developed from the curriculum for use with classroom teachers.

Results: The most significant area of coverage was for the Health and Physical education curriculum. The TFFK covered all of the safety requirements of the Ontario Health and Physical education curriculum mandate. Significant areas of coverage were also seen for subject areas such as mathematics, language, social studies and the arts.

Conclusion: The TFFK program meets provincially mandated educational reforms in multiple subject areas. The educational benefits of TFFK are likely to be multifaceted.

P-142

Long Term Follow-up of Treated Posttraumatic Syringomyelia: Role of Magnetic Resonance Imaging in the Evaluation of Outcome

E. Tsai, M. Fehlings, C. Tator (Toronto, Ontario)

Background: We sought to examine the value of magnetic resonance imaging (MRI) in the long term management of posttraumatic syringomyelia.

Methods: From our syringomyelia database of 141 cases, 25 patients (mean 44 yrs) with posttraumatic syringomyelia and preoperative MRI were assessed to correlate clinical outcome, change in syrinx size, and the need for further surgery.

Results: Initial surgical treatment included: syringopleural (n=12), syringosubarachnoid (n=7) or syringoperitoneal (n=2) shunts, or other (n=4). Mean clinical and MRI follow-up was 3.5 and 3.8 years, respectively. MRI initially showed syrinx size decrease in 18, increase in 2, and no change in 2. Postoperative MRI was not obtained in 3 due to metal artifact or patient refusal. Initial clinical results were improvement or stabilization in 16 and deterioration in 9. Of the 16 with improved or stabilized symptoms, 5 subsequently deteriorated (mean operation to deterioration time 8 months). All 14 patients with deterioration underwent further surgery. The MRI after deterioration or postoperative follow-up showed syrinx enlargement in 8, no change in 1, and a decrease in 3.

Conclusions: Long term clinical and MRI follow-up are essential in managing posttraumatic syringomyelia. Clinical deterioration may occur despite MRI evidence of cyst decompression suggesting other mechanisms of neural degeneration in these patients.

HISTORY

P-143

The Development of the Penfield Dissectors: An Untold Story

J.A. Shehadi, William Feindel (Montreal, Canada)

In 1928, Doctor Wilder Penfield went from New York to Breslau, Germany to work for 6 months with Professor Otfrid Foerster, who was then one of only a few neurosurgeons using brain mapping for epilepsy surgery. During this time, Dr. Penfield developed a series of 4 dissectors in collaboration with an unknown German "artisan instrument maker." They were practical and became widely used throughout the world. The first three dissectors were double ended. A special number 5 instrument, which was a longer version of the number 3 instrument with centimeter markings on it was used at the Montreal Neurological Institute and in Saskatoon to measure brain lesions and the extent of excision.

Little has been written on the first set, where they were made, the reason for making them, how the instruments later became mass produced and if and when they were patented. We summarize the current state of knowledge regarding these important neurosurgical instruments.

P-144

William Osler, the Rockefellers, and the Montreal Neurological Institute

William Feindel (Montreal, Quebec)

Background: On the 150th anniversary of William Osler's birth and the 65th anniversary of the Montreal Neurological Institute, this report summarizes how deeply these two events influenced the development of neurology, neurosurgery and neurosciences in Canada and beyond.

Methods: Sources consulted included the Osler Archives, Wilder Penfield Archive, the McGill Archives and the Rockefeller Foundation Archives.

Results:

1. William Osler, during the years 1872-1884 at McGill became Canada's first neuropathologist; his exhibit at Ottawa in 1880 sampled the range of his material.
2. Of Osler's 1400 publications, 250 related to neurology.
3. He knew Gowers, Jackson, Mitchell, Marie and Charcot, and through his support of Horsley and Cushing, promoted "medico-chirurgical neurology".
4. In 1919, a request from Osler resulted in the Rockefeller Foundation granting $5,000,000 to Canada's medical schools.
5. McGill's excellent decade of re-organization spurred by Rockerfeller funds set the stage for another grant in 1932 of $1, 250, 000 to establish the Montreal Neurological Institute.
6. Over the past 65 years the "Neuro" became recognized worldwide, particularly for the surgery of epilepsy, neuroimaging and molecular neurobiology. The new Brain Tumor Research Centre expands this field begun at McGill by Osler in 1872-1884.

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