1991
HALIFAX

XXVI[th] Meeting of the Canadian Congress of Neurological Sciences Halifax, June 1991 PROGRAM

Tuesday, June 18

Canadian Association for Child Neurology Annual Meeting

Morning

Issues for Methods in Clinical Research for Pediatric Neurologists

New Study Designs for Antiepileptic Medication	Joyce Cramer, New Haven
N of 1 Trials	Kevin Gordon, Halifax
Survey Questionnaires	Joseph Dooley, Halifax
Cohort Population Studies	Carol Camfield, Halifax
Multicentre Trials	Peter Camfield, Halifax

Afternoon

Movement Disorders in Children

Dystonia	Donald Calne, Vancouver
Peer Relationships in Children with Tourette Disorder	Harry Bawden, Halifax
Case Discussion of Movement Disorders in Children	Peter Camfield, Halifax

Wednesday, June 19

Morning

Congress Courses

COURSE 1: Mechanisms and Managements of Nerve Injuries

Chairs: Renn Hólness and Tim Benstead

Morning

Pathogenesis of Nerve Injury and Recovery	P.K. Thomas, London, England
Techniques and Science of Nerve Repair	David Kline, New Orleans
Place of Allographs in Peripheral Nerve Repair	Alan Hudson, Toronto
Controversy: Ulnar Neuropathy at the Elbow	
Introduction to the Problem	Tim Benstead, Halifax
The Case for Conservatism	John Stewart, Montreal
When to Operate and Which Operation	Alan Hudson, Toronto
Panel Discussion	

COURSE II: Movement Disorder Symposium

Chair: Ali Rajput

Morning

Opening Remarks & Epidemiology of Common Movement Disorders	Ali Rajput, Saskatoon
Tremor - Clinical Features, Diagnosis & Management	Leslie Findley, London, England
Current Management of Parkinsonism	William Koller, Kansas City
Common Varieties of Dystonia in Adults - Diagnosis & Management	Joseph Tsui, Vancouver
Classical and Not So Classical Features of Movement Disorders	Anthony Lang, Toronto
Panel Discussion	

COURSE III: Neuro-Ophthalmology

Chair: Charles Maxner

Morning

The Basic Neuro-Ophthalmologic Exam	Dan Boghen, Montreal
Acute Vision Loss	William Fletcher, Calgary
Assessment of Diplopia	Peter Savino, Philadelphia
Ocular Oscillations	James Sharpe, Toronto
Pupil Disorders	Charles Maxner, Halifax
Imaging in Neuro-ophthalmology	Peter Savino, Philadelphia
Questions and Closing Remarks	

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COURSE IV: Glioma: Bench to Bedside

Chair: David R. Macdonald

Afternoon

Biology and Genetics of Glioma	James Rutka, Toronto
Chemosensitivity Testing for Glioma	David Thomas, London
Brachytherapy for Glioma	Mark Bernstein, Toronto
Chemotherapy for Oligodendroglioma	David Macdonald, London

COURSE V: Headache

Chair: Robert Nelson

Afternoon

Introduction	Robert Nelson, Ottawa
The Trigeminovascular System and Headache	Michael Moskowitz, Boston
The Contribution of New Technologies to the Study of Headache	Michael Welch, Detroit
Migraine and Epilepsy	Peter Camfield, Halifax
The Application of New Understanding to the Treatment of the Headache Patient	John Edmeads, Toronto
Chronic Daily Headache, Possible Mechanisms	Robert Nelson, Ottawa

COURSE VI: EEG & Epilepsy

Chair: Sherrill Purves

Afternoon

EEG in Childhood Epilepsy	Warren Blume, London
EEG in Adult Epilepsy	Timothy Pedley, New York
The Technology of "EEG in the 1990's": Potential and Proven Applications	Jean Gotman, Montreal
Continuous EEG Monitoring: Clinical Applications and Results	Sherrill Purves, Vancouver
Review Panel with Audience Participation	Mark Sadler, Halifax

Thursday, June 20

Morning

PLENARY SESSION #1 - Guests of the Congress

Welcome

Opening of the Scientific Session

Richardson Lecture
P.K. Thomas, London, England
Guidance Factors in Nerve Regeneration

Penfield Lecture
David Kline, New Orleans
A Quarter-Century of Experience with Intra-operative NAP Recordings

Canadian Society of Clinical Neurophysiologists Lecture
Timothy Pedley, New York
Quantitative EEG and Topographic Mapping: One Neurologist's Perspective

"Meet the Expert" Lunch - Neurosurgery
David Kline, David Thomas

Afternoon

FREE COMMUNICATIONS

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Friday, June 21

Morning

PLENARY SESSION #2 - Guests of the Congress

Canadian Association for Child Neurology Guest Lecture
Harvey B. Sarnat, Calgary
Developmental Myopathies

Speaker of the Royal College of Physicians and Surgeons of Canada - Neurosurgery
David G.T. Thomas, London, England
Image Directed Neurosurgery

Special Communication
Henry J.M. Barnett, London
Early Results of NASCET

Afternoon

"Meet the Expert Lunch" - Adult Neurology
P.K. Thomas, Stephen Rothman

FREE COMMUNICATIONS

Saturday, June 22

Morning

PRESIDENT'S SYMPOSIUM
The Neurobiology of Excitatory Amino Acids in Plasticity and Neuronal Degeneration

Introductory Comments	Rick Riopelle, Kingston
Speaker of the Royal College of Physicians and Surgeons of Canada - Neurology	
Different Mechanisms of Cell Death in Neurological Disease and Development	Steven Rothman, St. Louis
Computational Exploration of the NMDA Receptor	Donald Weaver, Kingston
Excitatory Amino Acid Receptors are Targets of Modulation by Therapeutic Agents and Regulation by Intracellular Protein Kinases and Phosphatases	John MacDonald, Toronto
Neuronal Calcium Currents: Physiology and Pharmacology	Peter Carlen, Toronto
The Role of Calcium in Long-Term Potentiation	Kenneth Bainbridge, Vancouver

Afternoon

Canadian Stroke Society Guest Lecture
Vladimir Hachinski, London
Brain-Heart Interactions in Clinical Experimental Cerebral Infarction

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XXVIth Meeting of the Canadian Congress of Neurological Sciences

Abstracts of the Scientific Program

Platform Sessions

Poster Sessions

Platform Sessions

THURSDAY, JUNE 20, 1991 - P.M.

A. Neurosurgery

1.

Surgical Treatment of Asymptomatic Cerebral Aneurysms

W.B. WOODHURST and F.A. DURITY (Vancouver, British Columbia)

122 patients (pts) with asymptomatic cerebral aneurysms admitted to Vancouver General Hospital Jan. 1980 - June 1990 were reviewed.

27 pts (Group I) with symptomatic aneurysms had 47 asymptomatic aneurysms. 34 of these aneurysms were treated at the same craniotomy. There was no operative mortality and at 6 months 2 pts had mild deficits not attributable to the treatment of the asymptomatic aneurysms. Transient morbidity may have been increased in a few pts. 1 pt with an invasive pituitary adenoma and clipping of asymptomatic aneurysm, died of causes clearly related to the pituitary lesion.

23 pts (Group II) with 35 aneurysms underwent 26 surgical procedures after recovering from initial treatment for their symptomatic aneurysm (includes 7 pts, Group I). 34 of 35 aneurysms were treated, 1 small carotid ophthalmic aneurysm was not treated. There were no deaths in this group. 1 pt had very mild hemiparesis, 1 pt had mild but significant hemiparesis.

33 pts (Group III) with 48 asymptomatic aneurysms incidentally discovered underwent 38 operations treating 43 aneurysms. The 5 untreated lesions include 3 carotid cavernous aneurysms, 1 small basilarsuperior cerebellar aneurysm, 1 pt awaiting treatment. There were no deaths in this group but 2 pts had significant hemiplegia from vessel injury and 1 pt had a delayed severe ischemic optic neuropathy after clipping a large ophthalmic artery aneurysm.

We conclude that surgical treatment of asymptomatic aneurysms in pts presenting with a symptomatic aneurysm is generally well tolerated at the time of surgery for symptomatic lesion or remotely. Treatment of incidental asymptomatic aneurysms is generally safe but 2 significant complications were encountered in this group related to vessel injury. This group presents the greatest challenge in selection for surgical treatment.

2.

Effect of Surgical Manipulation on Primate Cerebral Arteries in Established Vasospasm

J.M. FINDLAY, R.L. MACDONALD, B.K.A. WEIR and M.G.A. GRACE (Edmonton, Alberta)

It is generally believed that surgery in the face of angiographic vasospasm (VSP) is dangerous due to an increased incidence of postoperative cerebral ischemia. One theory is that arterial narrowing is exacerbated by surgical manipulation of the vasospastic vessels during aneurysm dissection and clipping. This theory was tested in a primate model of cerebral VSP.

Six monkeys underwent baseline cerebral angiography, followed by induction of subarachnoid hemorrhage (SAH) on both sides of the circle of Willis. An equal amount of fresh autologous blood clot was placed around each internal carotid, anterior cerebral and middle cerebral artery. Six days later angiography was repeated and the right craniectomy was re-opened for clot evacuation and surgical manipulation of the right cerebral arteries, including placement of a temporary aneurysm clip on the right middle cerebral artery. The left cerebral arteries were not exposed or manipulated, and served as controls. Twenty-four hours later (day 7) angiography was

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repeated and the animals killed. Equal and significant VSP (> 30% reduction in vessel calibre compared to baseline, $p < 0.05$) was seen on both sides of the circle in all animals 6 and 7 days after SAH. There was no significant change in the severity of VSP on day 7 compared to day 6 in the right cerebral arteries. In this primate model manipulation of cerebral arteries in established VSP does not appear to worsen the degree of arterial narrowing measured 24 hours later. The increased risk of postoperative cerebral ischemia for surgery in the peak VSP period may be due to mechanisms other than increased arterial narrowing precipitated by surgical manipulation.

3.

Intracellular Free Calcium Concentration and Contractile Protein Change in Cultured Vascular Smooth Muscle Cells Following Prolonged Exposure to Oxyhemoglobin

Y. TAKANASHI, B.K.A. WEIR, B. VOLLRATH, H. KASUYA and R.L. MACDONALD (Edmonton, Alberta)

A cell culture of smooth muscle from monkey middle cerebral arteries was developed to allow quantitative assessment of intracellular calcium and immunofluorescence analysis during different periods of exposure to oxyhemoglobin. The time course of intracellular calcium concentration was examined for up to 7 days after exposure to oxyhemoglobin. Intracellular calcium concentrations were significantly elevated during exposure to oxyhemoglobin for 7 days ($p < 0.01$). The mean value for the control group was 75.2 ± 1.8 (nM) and immediately after application of oxyhemoglobin it rose to 239.5 ± 27.5 nM. After a single exposure to oxyhemoglobin the value returned closer to control levels on days 3 and 7. The intracellular calcium changes following multiple daily exposures to oxyhemoglobin were significantly greater than those increases following a single application of oxyhemoglobin on day 3 ($p < 0.01$), but there was no significant difference on day 7. Using immunofluorescence staining of FITC-labelled smooth muscle α-actin, smooth muscle cells exposed to oxyhemoglobin showed a reduction in immunoreactive α-actin. These data suggest that disruption of intracellular calcium regulation and calcium overloading may have crucial roles in the cell damage and cell death which may occur during cerebral vasospasm.

4.

Intracisternal rt-PA after Aneurysmal Subarachnoid Hemorrhage

J.M. FINDLAY, B.K.A. WEIR, N.F. KASSELL, L. DISNEY and M.G.A. GRACE (Edmonton, Alberta)

Fifteen patients undergoing surgery within 48 hours of aneurysm rupture were administered recombinant tissue plasminogen activator (rt-PA) directly into the basal subarachnoid cisterns after minimal surgical clot removal and aneurysm clipping. Preoperatively, 13 of 15 patients had diffuse or localized thick subarachnoid blood clots on computed tomography (CT), and 2 patients had diffuse thin clots. The rt-PA was given as a single 7.5 mg (1 patient), 10 mg (9 patients) or 15 mg (5 patients) intraoperative injection. Postoperative cisternal drainage was employed in 3 patients.

All patients except one demonstrated partial to complete cisternal clot clearance on CT within 24 hours. The patient who showed no clot reduction was the only patient to develop symptomatic vasospasm in this series, and was the only fatality dying 8 days after rupture. No vasospasm was seen on follow-up cerebral angiography in 6 of 15 patients, and mild to moderate arterial narrowing was seen in at least one major cerebral artery in the remaining 8 patients. Severe angiographic vasospasm was not seen, although the fatality in this series did not undergo repeat angiography. There was one major complication early in the series which seemed clearly related to treatment and that was a large extradural hematoma occurring within several hours of craniotomy. Intrathecal fibrinolytic treatment appears effective in clearing subarachnoid clot and reducing vasospasm, and may be associated with acceptable risks if given to patients with large volume SAHs at high risk for severe vasospasm.

5.

Is Angiographic Vasospasm a Contraindication to the Surgery?

M. BOJANOWSKY, A. ROUX, M. PARE, P. BOURGOUIN and C. JOLY (Montreal, Quebec)

The presence of cerebral angiographic vasospasm following subarachnoid hemorrhage is generally considered a contraindication to the immediate surgery of a ruptured cerebral aneurysm. The delay induced by the deferral of the surgery may be responsible of a rebleeding. During the three-year period from August 1987 through August 1990, 80 ruptured intracranial aneurysms have been treated microsurgically. The clinical, radiographical, surgical features and outcome of a series of ten patients with ruptured aneurysms operated upon despite angiographic vasospasm are presented.

Immediate preoperative clinical grades (Hunt & Hess) were between I and IV. Seven of the ten patients were operated between the fifth and eleventh days after the subarachnoid hemorrhage. Vasospasm just prior to operation was documented by cerebral 3 or 4 vessels angiogram. Six patients showed extensive and diffuse angiographic vasospasm, two multi-segmental and two local. All aneurysms were clipped using standard microsurgical technique and temporary clip application on parent vessels during aneurysmal dissection was used when necessary. Eight of the ten patients of this series have resumed their normal activities. One patient died of brain ischemia.

These preliminary results suggest that surgical treatment of ruptured intracranial aneurysms despite confirmed angiographic vasospasm offers favorable results.

6.

Aggressive Treatment of Poor Grade Patients With Ruptured Cerebral Aneurysms

M. PARE, M.W. BOJANOWSKI and C. JOLY (Montreal, Quebec)

In recent years, early surgery and aggressive medical treatment have been advocated following SAH by intracranial aneurysm rupture for patients in good clinical conditions. However, clinical decision making for patients in poor clinical condition upon arrival remains a matter of much debate.

In a retrospective study of 120 patients treated by the senior author (M.W.B.) at our institution between August '87 and

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December '90, we set out to evaluate the outcome of the 37 patients in poor clinical (26 Grade IV and 11 Grade V) Hunt & Hess on admission. Aggressive treatment included hemodynamic and intracranial stabilization, early surgery, and close postoperative monitoring of the intracranial pressure, cardiorespiratory and metabolic disorders.

Patients ranged in age from 33 to 68 years. There were 17 men and 20 women. All but two aneurysms were in the anterior circulation. On initial CT-scan, 21 patients were Miller-Fisher Grade IV, 16 were Grade III. Ten patients had acute hydrocephaly.

Sixteen patients in Grade IV upon arrival were operated within 48 hours of admission. At surgery, all aneurysms were clipped. Ten Grade IV and all Grade V patients died before they could be stabilized and operated. Rapid deterioration as a sequel of the initial ictus, uncontrollable intracranial pressure rebleeding and vasospasm were the main causes of death in the unoperated cases.

In the postoperative period, the PIC was rigorously kept under 20 cm/H_20 using standard protocols. Isovolemic hemodilution was successfully obtained in all patients and the arterial pressure was maintained between 90 and 110 mean pressure. Angiographic vasospasm was observed in six patients and became clinically significant in four patients.

Outcome in operated patients as graded by the Glasgow outcome scale at six months was good in 9 patients (Grade I and II), fair in four patients and poor in three patients. Three patients died.

The results of this study suggest that there is a subgroup of poor grade patients which can be stabilized and operated within 48 hours after SAH. The outcome of these patients is significantly better than the uniformly poor prognosis in patients not operated early. Therefore, aggressive medical treatment and early surgery should be attempted in poor grade patients as it represents a realistic chance of survival.

7.

The Relationship of Ventricular Drainage to Aneurysmal Rebleeding

L. PARE, R. DELFINO and R. LEBLANC (Montreal, Quebec)

Despite the widespread use of continuous external ventricular drainage (EVD) in patients with aneurysmal subarachnoid hemorrhage (SAH), the relationship of EVD to aneurysmal rerupture has not been fully investigated.

An historical cohort study of 128 subjects with confirmed aneurysmal SAH was undertaken using a multivariate stepwise logistic regression analysis to examine the relationship between aneurysmal rerupture and EVD, while controlling for important clinical and radiologic covariates. The covariates for EVD selected in the regression analysis were clinical grade, aneurysm size and hydrocephalus. The rate of rerupture (11.7% overall) was significantly higher with EVD (30%; odds ratio 5.31, 95% confidence interval 1.06, 26.67), poor clinical grade (odds ratio 4.90, 95% confidence interval 1.37, 17.49), and large aneurysm size (odds ratio 11.25, 95% confidence interval 1.78, 71.19). The significant effect of EVD was limited to subjects with radiologically-defined hydrocephalus (cerebroventricular index > 95th percentile for age).

It is concluded that EVD is associated with an increased risk of aneurysmal rebleeding, especially in the presence of hydrocephalus. Our data do not permit the inference that this relationship is causative, but could also suggest that the need for EVD, combined with hydrocephalus, poor clinical grade, and size of the aneurysm reflects a more severely disrupted aneurysm prone to rebleeding as part of its natural history.

8.

Normovolemic Hemodilution in the Perioperative Management of Good Grade Ruptured Aneurysms

A. TURMEL, A. ROUX and G. MOHR (Montreal, Quebec)

Controlled volume expansion and hypertension using invasive hemodynamic monitoring to improve the cerebral perfusion pressure, this reducing the deleterious effects of vasospasm, have become standard part of the perioperative management of S.A.H.

From January 1988 to December 31st 1990, 61 patients were operated on by the senior author for ruptured aneurysms. Although the majority of them had Swan-Ganz or CVP lines, 31 good grade patients were selected because of adequate hemodynamic monitoring values with Swan-Ganz catheters. Mean age of patients was 44.8 years (range 25 to 65 years). Patients were classified according to Hunt & Hess: 17 grade I, 7 grade II, 7 grade III. Eight patients were known hypertensive, one had diffuse atherosclerosis and one patient presented with cardiogenic pulmonary oedema.

Only three patients had pre-operative vasospasm shown by angiography. Early surgery (within 72h) was performed in 29 of the patients. One had late surgery (12 days post S.A.H.) and one was not operated on due to severe vasospasm. Medical treatment consisted of administration of crystalloids and colloids (albumin) to keep patients isovolemic with pulmonary diastolic pressures (P.D.P.) $\geq$ 14 to 18 mmHg and hemodiluted (hematocrit $\leq$ 33%). No induced hypervolemia ($\geq$ 18 mmHg P.D.P.) and only moderate hypertension were used. In our series, 29 out of 31 had a very good recovery, one had an important neurologic deficit, and one died of complications of vasospasm before operation.

These results, although preliminary, tend to show that in good-grade patients without known cardio-pulmonary pathology and in whom no vasospasm or moderate angiographic vasospasm exists, isovolemia and hemodilution may be adequate medical treatment, withholding aggressive "triple H" therapy for patients with severe post-operative vasospasm.

9.

Surgical Treatment of Arteriovenous Malformations Localized in Eloquent Regions of the Brain

M. PARE and M.W. BOJANOWSKI (Montreal, Quebec)

The localization of an A.V.M. in an eloquent region of the brain is considered a significant surgical risk potentially altering the choice of treatment.

We have retrospectively reviewed the outcome of 11 patients treated surgically for an A.V.M. in eloquent regions of the brain in the period of 1987-1990. The patients varied in age between 10 and 63 years old. Ten patients had presented an episode of intracerebral hemorrhage as the initial mode of presentation and one patient had convulsions. According to the Spetzler classification, an indication of the surgical risk, five patients were grade II, four were grade III, one was grade IV and two were grade V.

Complete surgical excision was possible in all patients and confirmed by postoperative angiography. There was no mortality. Three patients presented a slight temporary aggravation of their neurological deficit in the postoperative period and one patient presented a new temporary deficit.

These results indicate that the direct surgical approach is a safe modality of the treatment even for A.V.M. situated in eloquent areas

of the brain. The pertinent technical aspects permitting this approach are exposed and discussed.

10.

The Variable Presentations of Craniocervical and Cervical Dural Arteriovenous Malformations of the Spine

R.A. WILLINSKY, K.G. TERBRUGGE, P. LASJAUNIAS and W. MONTANERA (Toronto, Ontario; Paris, France)

The authors reviewed the charts and angiograms of four patients with dural arteriovenous malformation (AVM) in the upper spinal axis.

Two patients presented with dural AVMs at the craniocervical junction and two patients had dural AVMs in the lower cervical region. In three of the four patients, the diagnosis was not made until laminectomy. All patients were male, ages 36 to 57. One of the patients whose AVM was at the craniocervical junction presented with a slowly progressive thoracic myelopathy at T4. The other patient with an AVM at this location presented with tinnitus and a 6th nerve palsy. Both of these AVMs were fed predominantly by the ascending pharyngeal artery. One of the patients with a lower cervical dural AVM presented with a subarachnoid hemorrhage. The fourth patient presented with a progressive cervical myelopathy. This latter patient differed from the usual spinal dural AVM in that the venous drainage was predominantly extradural producing a compressive myelopathy. Two of the patients had a successful obliteration of their AVM by embolization. All patients showed clinical improvement by embolization.

Dural AVMs of the spine remain an elusive diagnosis. High resolution angiography of the craniospinal axis must be done to make the diagnosis and plan treatment. In the face of subarachnoid hemorrhage with negative cerebral angiogram, the diagnosis must be entertained if there are symptoms referrable to the spinal cord or roots.

11.

Intracranial Dural Arteriovenous Shunts Resulting in Venous Congestive Encephalopathy

W.J. MONTANERA, R. WILLINSKY, K. TERBRUGGE, L.N. DETILLY and M.C. WALLACE (Toronto, Ontario)

The clinical and radiologic data of 49 patients with cranial dural arteriovenous shunts were reviewed. These presented to the Toronto Western Hospital between 1984 and 1990. Thirty-two were dural arteriovenous malformations (AVMs) and 17 were carotid-cavernous fistulae. The focus of this report is to correlate associated cortical venous drainage (CVD) and/or venous occlusive disease to symptomatology.

The clinical presentation of 12 patients with cortical venous drainage included 2 patients with rapid onset dementia, 3 with subarachnoid hemorrhage, 1 with cerebellar infarction, 2 with parenchymal hematomas and 1 with hydrocephalus.

Direct venous pressure monitoring of the transverse sinus showed a significant pressure gradient in one encephalopathic patient with a dural AVM, cortical venous reflux and venous occlusive disease.

MRI in 2 patients with cortical venous drainage showed signal abnormalities of brain parenchyma as well as vessel (venous) dilatations.

We conclude that the presence of venous stenosis or occlusion in conjunction with a dural arteriovenous shunt may result in a venous congestive encephalopathy.

B. Neurosurgery

12.

Injuries to the Nervous System and Spine in Downhill Skiing

S.T. MYLES, N. MOHTADI and J. SCHNITTKER (Calgary, Alberta; Hamilton, Ontario)

This study documents injuries to the nervous system or spine from downhill skiing accidents, characterizes the skiers and the circumstances surrounding the injury. We reviewed the charts of downhill skiers admitted to the 3 University of Calgary teaching hospitals during a 5-year period, if the discharge diagnosis included injury to the peripheral or central nervous system, or spinal injury. The Office of the Chief Medical Examiner provided us with details about accidental deaths from downhill skiing, where nervous system trauma occurred, during the same time period. One hundred forty-five (145) downhill skiers sustained nervous system or spinal injuring during the study period. There were 5 deaths from nervous system trauma. In the 5-year period, there were 6,147,785 skier days recorded at the 11 ski areas involved, giving a rate of fatal nervous system injury of 0.8 per 1,000,000 skier visits. The mean age of the injured skiers was 23.8 years, and these injuries were 3 times more common in males than females. Eighty-eight (88) skiers sustained head injury, 25 had spinal fractures alone, 30 had spinal cord or nerve root injury, and 12 had peripheral nerve injury. The commonest method of injury was a simple fall on the hill, while collision with a tree was next in frequency, and accounted for the most severe injuries. Reckless skiing, design of ski runs and presence of man-made snow seemed to be contributing factors. The serious nature and number of these injuries needs to be recognized, and further study of casual factors and preventative measures undertaken.

13.

Pediatric Spinal Injury: 61 Deaths Over a 13-Year Period in Southern Alberta

M. HAMILTON and S.T. MYLES (Calgary, Alberta)

Pediatric spinal injury is uncommon and generally felt to represent only 5-10% of the total spinal injury population treated in hospitals. Lacking, however, is data concerning the role of spinal injury associated with traumatic death of the pediatric patient.

The records of the Chief Medical Examiner of Alberta, between January 1975 and December 1988 (13 years), were examined to identify all patients who had died with a component of spinal injury. A total of 427 subjects were identified, of which 61 (14.3%) were 17 years or younger. 32 were male and 29 female. 21 children were 0-9 years of age (34.4%). 14 children were 10-14 years of age (23%) and 26 were 15-17 years of age (42.6%). 35 of the injuries were fractures, 22 were fractures with evidence of spinal injury and 4 had spinal cord injury without evidence of fracture. Other details related to this patient population will be discussed. This identifies spinal injury as a significant factor in traumatic pediatric death.

14.

Head Injury in the Elderly

R.J. MOULTON, G. HOTZ, I. SULLIVAN, P.J. MULLER and W.S. TUCKER (Toronto, Ontario; Boston, U.S.A.)

Patients over 60 years of age form an increasing portion of the population and in future will constitute an increasingly important group of patients in neurosurgical practice. This paper reviews the outcome from head injury in patients 60 years of age and older.

Of 774 consecutive head injury admissions between Jan. 1986 and Dec. 1989, 165 occurred in patients ≥ 60 years of age. Patients in this age group were significantly more likely to be injured in falls, harbour intracranial mass lesions, and die from their injury than patients < 60 years old ($p = 0.000$) for all comparisons. The incidence of death exceeded 90% below a GCS of 5, 6, and 8 for patients in their 7th, 8th and 9th decades respectively. Survival increased past 50% at GCS 12 and 14 for patients in their 60's and 70's. Cumulative survival never exceeded 50% for patients in their 80's.

Survivors 60 years of age and older were significantly less likely to return home from hospital ($p = 0.000$). Less than 10% of patients were discharged home when the admission GCS was below 4, 6, and 15 for patients in their 7th, 8th, and 9th decades respectively. Survivors who were 70 or older had < 50% chance of discharge home for any level of injury severity. The average length of stay was 32 days for survivors over 60 who returned home, versus 55 days for those who were transferred to another institution.

It is hoped information from this paper will help in counselling families about the outcome from head injury in older patients, and in decisions about the appropriateness of heroic therapy in this age group. Preventative measures should be directed at prevention of falls in and around the home.

15.

Hyperventilation Induced Cerebral Oligemia and Ischemia in Patients With Severe Closed Head Injury

M. MATISHAK, M. MCDERMOTT, M. TWEEDDALE, J. RONCO, J. PROCIUK and J. FENWICK (Vancouver, British Columbia)

Objective: To determine whether moderate hyperventilation ($PaCO_2$ 25-35 mmHg) of patients with severe closed head injury produces cerebral oligemia or ischemia despite the maintenance of a cerebral perfusion pressure > 50 mmHg.

Methods: Thirteen mechanically ventilated adults with severe closed head injury (Glasgow coma score ≤ 8) were studied. Values were obtained for intracranial pressure, cerebral perfusion pressure, arterial and jugular bulb oxygen content and lactate concentration within 1 hour of ICU admission. Measurements were repeated 4 hourly for at least 48 hours. Cerebral oligemia was defined as a global cerebral oxygen extraction ratio ([arterial oxygen content-jugular bulb oxygen content/arterial oxygen content] x 100) of greater than 40%. Cerebral ischemia was defined as oligemia combined with an increased arterial-jugular bulb lactate gradient. Cerebral perfusion pressure was > 50 mmHg in all patients at the time of ICU admission.

Results: At the time of initial measurements 9 of 13 patients had cerebral oligemia and of these, 4 also had ischemia. In 6 of the 9 patients cerebral oligemia and ischemia were reversed by decreasing hyperventilation. There was no correlation between cerebral oligemia or ischemia and values of either intracranial pressure or cerebral perfusion pressure.

Conclusions: Even moderate hyperventilation of patients with severe closed head injury and adequate cerebral perfusion pressure can produce cerebral oligemia and ischemia detectable by monitoring global cerebral oxygen extraction and arterial-jugular bulb lactate gradients.

16.

Management of Vertebral Burst Fractures in Canada

J.M. FINDLAY, M.G.A. GRACE, L. SABOE and L. DAVIS (Edmonton, Alberta)

In burst fracture management the role of direct surgical removal of retropulsed bony fragments encroaching upon the spinal canal is controversial. Neurosurgeons and orthopedic surgeons across Canada were surveyed to determine current management of vertebral burst fractures, including use of direct surgical removal of retropulsed bony fragments. Willingness to participate in a study examining the effect of direct surgical decompression on long-term outcome was also ascertained.

A total of 69 of 101 surgeons polled responded (44/65 neuro, 25/36 ortho). In addition to plain X-rays most surgeons investigate burst fractures with computed tomography (97% neuro, 95% ortho), and about one-half of surgeons in each group repeat this investigation during or after treatment. Standard tomography is used less frequently in pretreatment assessment (40% neuro, 38% ortho), as is magnetic resonance imaging (17% neuro, 10% ortho) and myelography (14% neuro, 5% ortho).

Neurological condition significantly influences management of burst fractures. Neurologically intact patients with narrowing of the spinal canal are treated most often with stabilization only (57% neuro, 81% ortho, difference significant $P < 0.05$). The greater number of neuro-surgeons that directly decompress this type of patient (remove bony fragments) is balanced by the number of orthopedic surgeons that believe that certain internal stabilization methods are able to reduce burst fractures and indirectly decompress the spinal canal. Patients with partial, stable neurological injuries are usually managed by direct decompression of the spinal canal and stabilization (83% neuro, 76% ortho, difference not significant).

About one-half of the surgeons polled would be willing to participate in a randomized study comparing direct surgical decompression plus stabilization versus stabilization alone in both neurologically intact and partially injured patients with burst fractures. Such a randomized study is necessary to determine whether direct bony fragment decompression, in addition to stabilization alone (with or without a tendon indirect decompression) yields better long term results.

17.

Wilder Penfield, Surgeon-Scientist (1891-1976) — A Centennial Appreciation

W.H. FEINDEL (Montreal, Quebec)

Wilder Penfield was recognized for two major accomplishments — his scientific and surgical contributions to the development of the successful surgical treatment of focal epilepsy and the founding and direction with many associates of the Montreal Neurological

Institute as a world centre for teaching, treatment and research related to the brain and nerves.

His writings ranged widely from neuropathology and neurocytology (30 papers), to epilepsy (46), cerebral localization (44), biography and history (50), neurology and neurosurgery (70), and included general topics such as language education, the importance of the family, government support of university research, the significance of endowment and the second career.

His reports in neurology and neurosurgery alone covered the gamut of many basic and clinical aspects of the nervous system. They included the physiology of the nervous system, neurocytology, radiology, cerebral circulation, anatomical and surgical features of headache, localization of speech and memory in the human brain, the supplementary motor region, the psychological signif-icance of the frontal lobes, a long series of studies on the function of the temporal lobe, many technical papers on surgery of the nervous system and finally his abiding interest in the brain, consciousness and the mystery of the mind.

An outline of his work and some assessment of its significance to neurology and neurosurgery in Canada and at large will be presented.

18.

Lumbosacral Plexopathy: Diagnostic Implications

E.G. DUNCAN, B.G. BENOIT and P. BOURQUE (Ottawa, Ontario)

Lumbosacral plexopathy (LSP) is usually a secondary phenomenon in patients with diabetes, malignancy or inflammatory disorders. In 1981 "idiopathic" cases were first described. LSP causes leg pain, with variable motor/sensory signs, and may mimic disc or spondylotic disease, leading to diagnostic error and inappropriate surgical treatment.

The clinical features of LSP at the Ottawa Civic Hospital were reviewed for the years 1985/90. Of the 21 cases, 4 were diabetic, 5 had malignancy, 1 had both and 11 were labelled as "idiopathic" after investigation. One iatrogenic case followed resection of a pelvic tumor. The mean age was 66 years and the male/female ratio was 1:2.5.

The initial misdiagnosis was frequent especially in the idiopathic group. Symptoms were often ascribed to neurogenic claudication secondary to spinal stenosis or radiculopathy secondary to disc herniation.

LSP was a presenting feature in 20% of the patients with malignancy and 25% of the patients with diabetes. The blood glucose level was elevated in 73% of the idiopathic cases. In the 15 diabetic or idiopathic patients the ESR was elevated in 92%. Accurate diagnosis requires full imaging of the spine and pelvis (CT, myelography, MRI, ultrasound) combined with electrophysiological studies.

A careful assessment is required to prevent unnecessary operations as many of these patients have incidental spinal degenerative disease. Also, judicious investigations may lead to the diagnosis of previously unrecognized diabetes or malignancy.

19.

Adult Diastematomyelia

N.A. RUSSELL, B.G. BENOIT, A.J. JOAQUIN and N. AL FAYEZ (Ottawa, Ontario; Riyadh, Saudi Arabia)

Adult diastematomyelia (DM) usually presents with a well recognized syndrome of neurological and musculoskeletal abnormalities. Recently, the syndrome has been recognized in adults, with increasing frequency.

We present a case of DM in a female of 41 years, who developed symptoms after an accident. Forty-two other cases were retrieved from the literature, and fully reviewed. Definite traumatic incidents that precipitated symptoms were identified in 15 patients. Twelve had minor musculoskeletal or neurological deficits from childhood, and 19 had cutaneous stigmata suggestive of spinal dysraphism.

Pain in the back and legs followed by sensory motor deficits and bladder dysfunction, were common. Plain radiographs showed a variety of congenital spinal abnormalities. Metrizimide myelography with computerized tomographic (CT) scanning was the most useful investigation. Decompression of the neural elements by removing the bone spur and associated adhesions, resulted in improvement in the majority of patients. Modern surgical techniques applied early, are effective in preventing neurological deterioration in adults with DM.

20.

The Disproportionately Enlarged 4th Ventricle

J.-G. VILLEMURE and D. MELANSON (Montreal, Quebec)

In the past 10 years, the authors have encountered 5 cases of patients suffering from hydrocephalus where the radiological investigation demonstrated disproportionately enlarged 4th ventricle.

All patients presented gait difficulties which might have been related to hydrocephalus itself. Some patients did present with hypertensive hydrocephalus while others had normotensive hydrocephalus. Headache was a prominent feature in most of the patients. The story was short (2 months) to more than one year. Four out of 5 patients presented rotatory nystagmus which is not a feature usually encountered in hydrocephalus and is interpreted as reflecting direct pressure on the floor of the 4th ventricle.

The radiological investigation was characterized by diffuse ventricular enlargement with a markedly enlarged 4th ventricle out of proportion to what is usually seen in hydrocephalus. With contrast study by ventriculography and cisternography, occlusion of the outlet of the 4th ventricle was demonstrated in a few cases. All patients were treated by suboccipital craniectomy and in all instances occlusion of the foramen of Magendi by tonsils or membrane was encountered and dealt with.

We believe that disproportionately enlarged 4th ventricle has a specific clinical presentation, is associated with very clear radiological features and should be treated preferably not by shunting procedure which could lead to sequestration of the 4th ventricle but rather by exploration of the posterior fossa and creation of an outlet of the 4th ventricle.

21.

Spinal Epidural Abscess: Trends in Diagnosis and Management

G.J. REDEKOP and R.F. DEL MAESTRO (London, Ontario)

Twenty-five patients with spinal epidural abscess were treated at the University of Western Ontario hospitals between July 1980 and July 1988. Twenty cases were classified as acute, with frankly purulent epidural collections; five cases were chronic, consisting of

epidural granulation tissue. Staphylococcus aureus was the most common etiologic agent, being isolated in 72% of the abscesses.

The progression from back and radicular pain to weakness and eventual paralysis continues to be characteristic of spinal epidural infection. Morbidity and mortality remain unacceptably high because of the delay in diagnosis and treatment. A grading scheme based on the clinical status at the time of presentation is proposed and the importance of early recognition of symptoms and signs is emphasized. Magnetic resonance imaging is the imaging modality of choice in the diagnosis of spinal epidural abscess and its impact on diagnosis and outcome is discussed.

22.

Neurosurgical Operative Diagnoses in the Elderly: A Cohort

A.L. AMACHER (Danville, U.S.A.)

During a 36-month interval (07/87 through 06/90) 298 of 2,427 consecutive neurosurgical operations (12.3%) were done on patients in the eighth, ninth, and tenth decades of life. The patient cohort (272) is derived from a rural and stable population in which long-term follow-up is accurate. This presentation will document operative diagnoses, early outcomes, and operative mortalities. It is intended to follow this cohort until all members are dead, in order to acquire information on cost-effectiveness of various surgical therapies in this age group which is becoming a larger and more active part of the social body.

Of 240 procedures done on septuagenarians, lumbar stenosis (50) and brain tumors (40) were the most common diagnoses. In the ninth decade (53 cases), the most common diagnoses were chronic or subacute subdurals (21) and brain tumor (6). All 5 diagnoses in nonagenarians were chronic subdurals. In the cohort, 23 patients have had ruptured discs, most of them with extra-annular fragments. There have been 5 aneurysms clipped and 2 angiomas removed very successfully. Overall, males predominate 153/145 for procedures, 141/131 for patients. The operative mortality for all spinal and nonemergent cranial procedures has been 0.

C. Movement Disorders

23.

Impact of Levodopa on Survival in Parkinsonism

A.H. RAJPUT, R.J. UITTI, K.P. OFFORD, A. RAJPUT and P. BASRAN (Saskatoon, Saskatchewan)

Soon after the introduction of levodopa (LD), it was suggested that survival in Parkinson's disease patients treated with this drug will increase. Several studies have reported normal life expectancy in LD treated cases while others have failed to confirm that. This issue is hard to resolve as contemporary untreated patients are not available for comparison with the treated group. Life expectancy in the general population has increased over the last four decades, therefore comparison with the retrospective data is inappropriate.

934 Parkinsonian (PS) cases with an average 9.3 year follow-up seen between 1968-1990 formed the basis of this report. The mean duration of illness at the first visit was 5.5 years and median survival after that was 10.3 years. Age at onset, disability at first visit and the type of PS in our cases were comparable with a large population based study in Finland and a clinic based study by Hoehn & Yahr (1967). The majority (77%) of our patients were treated with levodopa. Based on the type of PS, the cases were further divided into ever and never treated with LD. Survival in each subgroup was compared with the sex and date of birth matched cohort of the regional population from the index date of first clinic visit. The survival in all PS cases, idiopathic Parkinson's disease, levodopa treated and levodopa untreated subgroups, each was significantly shorter than expected. The mean survival prior to levodopa was 9.4 years and is now more than 15 years. It is still reduced compared to general population and the improved survival cannot be attributed to levodopa therapy. Implications of these observations to the prevalence rate, the basis of improved survival and the reasons for contradictory literature results will be discussed.

24.

A Population Based Case-Control Study of Parkinson's Disease and Exposure to Rural Occupational and Environmental Factors

K.M. SEMCHUK, E.J. LOVE and R.G. LEE (Saskatoon, Saskatchewan; Calgary, Alberta)

A population based case-control study was conducted in the city of Calgary in 1989 in order to determine whether exposure to rural occupational (agricultural work and chemicals) or environmental (rural living and well water drinking in childhood) factors lead to an increased likelihood of developing Parkinson's disease.

Cases (n = 130) with idiopathic Parkinson's disease, confirmed by a neurologist, were identified through contacts with the city's 5 general hospitals, 24 longterm care facilities, 16 neurologists, the Movement Disorder Clinic, and the Parkinson's Society. Two matched (by sex and age ± 2.5 years) community controls were randomly selected for each case by random digit dialing. Lifetime residential and occupational histories, including information on work-related chemical exposures, were obtained by personal interviews. The data were analyzed using conditional logistic regression for matched sets.

A significant ($p < 0.05$) two-fold or greater increase in risk for Parkinson's disease was associated with occupational exposure to: field crop farming, grain farming, herbicides, insecticides, and synthetic fertilizers. A dose-response relation was observed between the risk of developing Parkinson's disease and the cumulative lifetime exposure to field crop farming and to grain farming. No significant increase in risk for Parkinson's disease was associated with a history of rural living or childhood well water drinking (during the first 15 years of life or at any time during the first 45 years of life), or occupational exposure to market gardening, wood processing, or fungicide use. Multivariate conditional logistic regression was used to estimate the risk associated with each potential risk factor while controlling for the effects of the other factors, and to test for interaction between factors. Only previous occupational herbicide use was associated with a significant increase in risk for Parkinson's disease (odds ratio = 3.47, $p = 0.038$) in the multivariate analysis.

These data concur with the results of previous epidemiologic studies of Parkinson's disease and with case reports of chronic central and peripheral nervous system dysfunction in pesticide-exposed grain workers. Hence, the hypothesized involvement of an environmental toxin in the etiology of Parkinson's disease is supported.

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25.

Neurotoxicity of Identified Weed Extracts: Implications for Parkinson's Disease

R.J. RIOPELLE, R.J. BOEGMAN, C.M. WRAY, P.B. LITTLE and K.L. STEVENS (Kingston, Ontario; Guelph, Ontario; Albany, U.S.A.)

Extracts of a widely distributed family of weed (*Asteraceae*) produced dose-dependent toxicity to neurons *in vitro*. Of a group of sesquiterpene lactones purified from *Acroptilon repens* (Russian knapweed) and *Centaurea solstitialis* (yellow star-thistle), repin displayed the highest rank ordering of toxicity with a 50% toxic dose (TD50) of 80 nM, while the C-17 epimer subluteolide had a TD50 of 300 NM. Five other sesquiterpene lactones were slightly less toxic than subluteolide with TD50's ranging between 350-800 nM. Direct inoculation of repin to the rat striatum produced neuronal and glial toxicity which was maximal between 20-100 nmol. The neuronal toxicity included swelling of cell bodies, varicose enlargement of processes, and cell loss. The sesquiterpene lactones may be implicated in the pathogenesis of equine nigropal-lidal encephalomalacia (ENE), a disorder with some clinical features similar to human parkinsonism. Toxicity associated with extracts of the *Asteraceae* family of week may provide clues to support data emerging from analytic epidemiologic studies that suggest a role for rural factors in production of certain neurodegenerative diseases.

Supported by the Parkinson Foundation of Canada.

26.

Cholecystokinin Modifies the Response to Levodopa in an Animal Model of Parkinson's Disease

A.J. STOESSL and E. SZCZUTKOWSKI (London, Ontario)

The treatment of Parkinson's disease with levodopa is complicated by the development of distressing involuntary movements or dyskinesias. There is considerable anatomical, biochemical, physiological and behavioural evidence for significant interactions between cholecystokinin (CCK) and dopamine within the central nervous system, and levels of CCK immunoreactivity are decreased in Parkinsonian substantia nigra. We have therefore studied the effects of centrally administered CCK on the response to levodopa in a rodent model of Parkinson's disease.

Male Sprague-Dawley rats were pretreated with pargyline and desipramine, and 6-hydroxydopamine (6 ug/2 ul) was then infused into the medial forebrain bundle bilaterally. Guide cannulae were simultaneously implanted into the lateral ventricles. Following recovery from surgery, animals were pretreated with carbidopa (25 mg/kg IP) and then received a range of doses (0-50 mg/kg IP) of levodopa, followed 15 minutes later by CCK (50 ng ICV) or its vehicle (0.9% saline). Behavioural responses were then recorded by direct observation for 80 minutes.

In sham-lesioned animals, levodopa increased locomotion as expected, an effect that was suppressed by CCK. In the lesioned animals, the emergence of stereotyped behaviour resulted in *suppression* of locomotion by levodopa, an effect that was reversed by CCK. In contrast, levodopa did not affect grooming in the sham-lesioned animals, but evoked intense self-injurious grooming in the lesioned animals, an effect which was suppressed by CCK.

These findings suggest that CCK suppresses the undesirable effects of levodopa (analogous to dyskinesias) in animals with destruction of the dopamine projections, and converts the behavioural responses in these animals to a normal profile. Thus, CCK-like compounds may be beneficial in the long-term management of Parkinson's disease.

27.

Neurochemical Abnormalities in Huntington's Disease Cerebral Cortex May Occur Independently of Striatal Atrophy

M.F. MAZUREK and P.I. ROSEBUSH (Hamilton, Ontario)

Huntington's disease (HD) is an autosomal dominant disorder characterized by progressive involuntary movements, psychiatric disturbances and dementia. While the choreoathetotic movement disorder is quite clearly related to the extensive atrophy of spiny neurons in the striatum, the morphological and neurochemical basis of the neuropsychiatric deterioration observed in HD patients has not been elucidated. We have studied levels of neuropeptide immunoreactivity in 13 cases of postmortem cerebral cortex dissected from 24 cases of HD and 12 controls. Concentrations of cholecystokinin (CCK) were consistently elevated by 57-123% in HD cerebral cortex, with levels averaging 88 ± 6% (mean ± standard error of the mean) above control values. Vasoactive intestinal polypeptide (VIP) and neuropeptide Y (NPY) were also increased, by 51 ± 8% and 57 ± 8% respectively. Changes in somatostatin were less consistent, with mean levels 24 ± 6% higher than control values. Substance P was for the most part unchanged, mean levels in HD cortex being only 10 ± 3% above those of controls. There was no relationship whatever between the increases in cortical peptide levels and the degree of striatal atrophy. In a separate series of experiments, extensive chronic striatal lesions in rats failed to produce the cortical peptide changes observed in HD. Taken together, these findings suggest that the widespread neuropeptide changes in HD cerebral cortex may not simply be a consequence of abnormal input from the degenerating cortical-striatal-pallidal-thalamic feedback circuit.

These results indicate that the neurochemical abnormalities associated with HD are not confined to the striatum, and raise the possibility that the neuropsychiatric disturbances of HD may not simply be subcortical in origin.

28.

Dopamine Receptor Blockade Can Attenuate Excitotoxin-Induced Tissue Damage in the Striatum

M.F. MAZUREK, S. GARSIDE and P.I. ROSEBUSH (Hamilton, Ontario)

Excitotoxicity mediated by the NMDA receptor has been implicated in neuronal damage associated with such disorders as stroke, epilepsy and Huntington's disease. We have investigated the ability of the dopamine D-2 receptor antagonist haloperidol to modify NMDA-mediated toxicity in the striatum. The specific NMDA agonist QUIN was injected into the right striatum of rats pretreated with one of: (1) saline (controls); (2) haloperidol 0.2 mg/kg (LOW HAL); (3) haloperidol 2.0/kg (HIGH HAL); (4) 6-OH DA lesion of the nigrostriatal tract. Animals were sacrificed by decapitation 7 days later. Brains were sliced in the coronal plane and photographed. Lesion size was estimated using two measures: ranking of lesion size from photographs by blinded observers; and quantitation of lesion using the Bioquant II programme. The size of the lesion was significantly attenuated by both measures in the HIGH HAL

and the 6-OH DA groups. LOW HAL animals had lesions comparable to those of controls.

These results suggest that dopamine D-2 receptor activation is important for the expression of excitotoxicity in the striatum. Haloperidol might help prevent neuronal damage in stroke and Huntington's disease.

29.

Benefits and Side Effects of Deprenyl: A Survey

O. SUCHOWERSKY, G. ROHS and C. DEMONG (Calgary, Alberta)

Deprenyl has been available for the treatment of Parkinson's disease (PD) by prescription in Canada for 1 year. It has received much publicity in the lay press with claims that it increases energy level, feeling of well being and sexual drive, and has few side effects.

Over the past year, as our patients with PD have been started on deprenyl, we administered a short questionnaire specifically looking at these issues. Ninety-one patients were surveyed, 16 of which were not taking other anti-PD medications. A total of 31 (34%) had side effects, consisting of GI upset, insomnia, agitation, hallucinations and dyskinesias. Although most patients improved following decrease in dose, 13 patients (14%) had to discontinue the drug due to severity of side effects.

Of the 16 de novo patients, 6 (38%) had some improvement in energy level and general well being. Two of these also reported an improvement in PD. In L-dopa treated patients 34 (45%) reported some improvement in PD. Only 7 (9%) reported an increase in energy level (reported as mild), which could not be attributed to improvement in Parkinsonism.

A total of 11 patients (12%) reported an increase in sexual drive: this was usually mild, and related to improvement in Parkinsonian symptoms or energy level.

Deprenyl has been shown to be a valuable drug in the treatment of PD. However, a significant number of patients developed side effects on the recommended dose (5 mg b.i.d.).

There was no significant improvement in energy level in most L-dopa treated patients. When it did occur, it was usually related to improvement in PD. In de novo patients, almost 40% did report an improvement in energy level or well being. The cause of this is unclear. No patient reported a significant or specific benefit with respect to sexual drive.

30.

Botulinum Toxin in Writer's Cramp: A Double-Blind Study

J.K.C. TSUI, M. BHATT and D.B. CALNE (Vancouver, British Columbia)

We studied 20 patients with focal dystonia of the hand who had symptoms only when they were writing. Each patient was given 2 series of injections at an interval of 3 months. One of the treatments consisted of intramuscular injections of botulinum-A toxin (BTX-A) and the other normal saline (placebo). The order of treatment was unknown to the patients and the physician performing the injections and assessments. The patients were seen 2, 6 and 12 weeks after each therapeutic procedure. The forearm muscles were studied with wire electrodes before treatment, to facilitate selection of the most active muscles, which included the flexor digitorum superficialis, flexor digitorum profundus, flexor carpi ulnaris, extensor digitorum, and extensor carpi ulnaris. The dose of BTX-A varied from 10 to 50 mouse units (4 to 20 ng) per muscle. At each visit, the patients were tested for pen control by (1) computer-aided objective measurements of speed and accuracy of movement, (2) tracing patterns on paper, and (3) writing standard passages. The results showed that compared to placebo therapy, computer measurements of speed and accuracy of pen control improved in 12 patients 6 weeks after treatment with BTX-A, tracing patterns improved in 9, and writing improved in 7. There was no significant difference between initial base line values and those obtained after placebo injections. No side effects were experienced. We conclude that BTX-A injections are effective in relieving symptoms in selected cases of writer's cramp. The clinical feature most useful in predicting the outcome to treatment was significant distortion of wrist posture while writing.

31.

Treatment of Spasmodic Torticollis with Botulinum Toxin

D.R. BOGHEN and M. FLANDERS (Montreal, Quebec)

Recent reports on the treatment of patients with Spasmodic torticollis (SD) show favorable responses using local injections of Botulinum toxin. Standardized assessment of patients for the purpose of evaluating results of treatment has been difficult to achieve.

In this study, 32 patients with SD were assessed quantitatively for posture deformity, tremor and range of neck movement, and qualitatively for pain and global subjective disability. All patients were then treated with intramuscular Botulinum toxin injections into appropriate neck muscles. Fifty-three injection sessions were completed using dosages of toxin in the range of 75 to 400 units. The progress of the patients was assessed during an 18-month period.

Seventy-five percent of patients showed documented improvement in both subjective and objective parameters and were considered treatment successes. Pain improved in 65%, posture in 65%, tremor in 50% and range in 46%. Side effects that occurred were transient and included fatigue, dysphagia, neck weakness, hoarseness and local pain.

This study demonstrates that treatment with Botulinum toxin is of significant benefit for the majority of patients with spasmodic torticollis.

32.

4.0T Magnetic Resonance Imaging (MRI) of Brain Iron in Healthy Controls

J.F. SCHENCK, C.L. DUMOULIN and W.E. KOZACHUK (Schenectady and Columbia, U.S.A.)

We present a prospective study on the safety of 4.0T high field imaging and its potential use in imaging brain iron. MRI scanning of up to 35 hours in healthy controls (HC) revealed no adverse side effects other than subjective sensations of nausea, vertigo and metallic taste when head movement occurred at 4.0T field strength.

Iron concentrations are increased in the basal ganglia and increase with normal aging (Hallgren *et al.* J Neurochem 1958; 3: 41-51). MRI scans in both HC and neurological disease at 1.5T reveals a T2 signal loss corresponding to areas of increased iron concentration. Since the MRI signal increases linearly with field

strength 4.0T MRI predicts superior resolution of the basal ganglia and localization of brain iron. In HC, increased contrast and resolution was evident in the basal ganglia plus the pulvinar, the latter area not well delineated at 1.5T.

We conclude that 4.0T MRI provides superior resolution of the paramagnetic effects of brain iron. Since abnormal distribution and metabolism may contribute to the pathophysiology of neurologic disorders (Dexter *et al.* J Neurochem 1989; 53:1830-36), 4.0T imaging promises superior diagnostic and investigative potential in neurological disease, specifically in movement disorders.

33.

4.0T Magnetic Resonance Imaging in Familial Inverted Chorea (FIC)

W.E. KOZACHUK, J.F. SCHENCK and C.L. DUMOULIN (Columbia and Schenectady, U.S.A.)

We present the first clinical study of a neurological disease in a 58 y/o male using 4.0T MRI. FIC, a rare autosomal dominant disorder, is characterized by lower extremity chorea and normal cognition. Previous 18FDG-PET scans revealed no reduction in caudate metabolism (Petrini *et al.* Soc N Med 1990; p. 16).

We compared MRI images of the basal ganglia at 0.5T, 1.5T, and 4.0T field strengths. T1 and T-2 weighted (TR 2000, TE 20/40/60/80) images of 3mm thickness, field of view 24 cm and imaging matrix 128x256 were obtained.

MRI revealed no caudate or cortical atrophy. 0.5T MRI had minimal resolution of the basal ganglia with no T2 signal loss. 1.5T images revealed signal loss in the putamen and medial globus pallidus (GP) but increased T2 signal loss and superior resolution of the putamen, GP, red nucleus and substantia nigra was evident at 4.0T MRI.

We conclude that 4.0T MRI provides enhanced contrast of iron containing subcortical nuclei which may improve the future diagnosis of movement disorders. 4.0T MRI may also provide anatomical correlation of the basal ganglia with future ligand-receptor PET studies.

34.

Reduced Serum Iron in Neuroleptic Malignant Syndrome: Implications for Pathophysiology

P.I. ROSEBUSH and M.F. MAZUREK (Hamilton, Ontario)

Neuroleptic malignant syndrome (NMS) is a fulminant, life threatening reaction to neuroleptic medications. Clinical features include fever, delirium, rigidity, diaphoresis, tremulousness, blood pressure abnormalities and tachycardia. The only consistently described biochemical abnormality has been an elevated creatine phosphokinase (CPK). We report that virtually all cases of NMS are accompanied by a marked decrease in serum iron (Fe). To date we have studied 31 consecutive cases of NMS and have measured serum iron in 26. In 25 of the 26 cases (96%) levels of serum iron fell below the lower limit of the normal range (55-180 μg/dl = mean ± 2 SD). The serum iron in 9 (36%) fell to 20 μg/dl or below. In the lone patient whose values remained within the normal range the serum iron on five determinations during the NMS episode was 83 ± 9 (mean ± SD) as contrasted with 132 ± 9 following recovery. In each case for which data are available the serum iron returned to normal levels upon resolution of the NMS. Where multiple data points were available, there was a negative correlation between levels of serum iron and concentrations of CPK.

The consistent finding of low serum Fe raises the possibility that the pathophysiology of NMS may involve a massive release of acute phase proteins, particularly interleukins 1 and 6, both of which are known to produce fever, leukocytosis, muscle breakdown and hypoferraemia. Since iron is known to be essential for the normal function of the D2 receptor, it is possible that low serum iron may in turn contribute to the pathophysiology of NMS, in addition to being a marker for the disorder.

D. Epilepsy

35.

Temporal Lobectomy Follow-up Study Using Detailed Epilepsy and EEG Data Base Systems

H. DESAI, W.T. BLUME, J.P. GIRVIN, J.F. LEMIEUX and R.S. MCLACHLAN (London, Ontario)

Using a detailed epilepsy and EEG database permitting multiple correlations, we report the first study of year-by-year seizure control among 125 patients after temporal lobectomy for each seizure type: complex partial (CPS) and grand mal (GM).

Among 80 patients with CPS and GM preoperatively, for all years, temoral lobectomy gave ≥ 90% control of CPS in 87% and GM in 76%. Lack of preoperative GM improved such CPS control: from 87% (with) to 98% (without). However, 14 of 80 patients (17%) obtained no improvement in GM control.

Comparing final follow-up year data with those of preceding postoperative years indicates efficacy improves with time for each seizure type. For example, ≥ 90% control of CPS occurred in 89% at two years, 95% at the final year, and 91% overall in all 125 patients with CPS with or without GM preoperatively.

Despite highly favourable outcomes (above) 44% of patients with CPS + GM preoperatively had at least one seizure of either type after operation while 18% of patients with only CPS preoperatively did so.

One or more scalp and/or subdurally-recorded seizures from the contralateral temporal lobe reduces CPS and GM seizure control.

36.

Hemispherectomy in Chronic Encephalitis

J.G. VILLEMURE, F. ANDERMANN and T. RASMUSSEN (Montreal, Quebec)

Twenty-one (21) patients suffering from chronic encephalitis and seizures underwent hemispherectomy for control of medically refractory seizures. 33% presented epilepsia partialis continua while the others exhibited multiple seizure patterns. There were 12 males and 9 females; age at surgery ranged from 3 to 29 years of age. There were 11 right and 10 left hemispherectomies. 11 patients had the hemispherectomy done in one stage while 10 had it in 2 to 4 stages. There were 8 anatomical and 13 functional hemispherectomies. Complete seizure control was obtained in 12 patients (58%), while 19 of 21 patients showed more than 80% improvement in seizure frequency. Two patients were operated prior to maximal motor deficit.

Timing of surgery in this condition remains an issue as well as the surgical modality. Focal resection appears to have little benefit. The progression of the neurological deficit may guide the medical and surgical therapy. Corticosteroids or immunoglobulins may be worth trying in slow progressive disease. Hemispherectomy should not be considered in patients with mild stable hemiparesis; it should be recommended when the patient presents a severe hemiparesis; in the absence of a maximal motor deficit, but in the presence of a progressive hemiparesis, where the rate of progression indicates the development of a severe motor deficit in the near future, early hemispherectomy should be seriously considered.

37.

Memory Loss After Internal Carotid Artery Injection of Sodium Amytal is not Related to Filling of the Posterior Cerebral Artery

I.M. SMITH, J. MCGLONE and A. FOX (Halifax, Nova Scotia; London, Ontario)

Jack et al (Radiology, 1988) advocated injection of sodium amytal directly into the posterior cerebral artery (PCA) rather than internal carotid artery (ICA) for the selective examination of memory functions prior to temporal lobectomy. The higher risk procedure was believed to inactivate the posterior hippocampus, thus improving prediction of post-surgical memory loss. Milner, however, claimed that filling of the PCA was not necessary to produce global amnesia. To date, no empirical evidence exists to address this critical issue. We examined the relationship between filling of the PCA and recognition memory in 81 epileptic patients with a unilateral temporal lobe seizure focus. Angiography was performed by hand injection just prior to the ICA administration of 175 mg sodium amytal. Later, degree of filling of the main cerebral arteries was rated blindly on a 4-point scale from 0 (no filling) to 3 (completely filled). No significant correlations were found between degree of filling of the PCA and recognition memory scores when the injection was contralateral to the major temporal lobe seizure focus ($r = -.05$), or ipsilateral ($r - .09$). Using a pass/fail cut-off, the percentages of patients with transient global amnesia did not differ between patients with and without filling of the contralateral PCA (61% and 60%, respectively). Assuming that the distribution of the dye, this study found no evidence that filling of the PCA had any impact on the occurrence or degree of memory loss following ICA sodium amytal injection.

38.

Electrical Stimulation of the Vagus Nerve During Penicillin-induced Focal Interictal Spike Activity

R.S. MCLACHLAN, F. BIHARI and J.W. CRUICKSHANK (London, Ontario)

Chronic intermittent stimulation of the vagus nerve has been suggested as a new approach for the treatment of patients with intractable partial seizures. However, only a few studies of this technique have been carried out in animal models of epilepsy. Focal epileptiform activity was established in the somatosensory cortex of 12 urethane anaesthetized (1.5 gm/kg) rats by direct application of potassium penicillin G (100,000 IU/ml) to the left hemisphere. The electrocorticogram, electrocardiogram, and respiration were recorded continuously. When focal interictal spike activity was well established, electrical stimulation of the exposed left vagus nerve in the neck was carried out using a bipolar electrode (0.1-1.2 mA, 10-50 hz, 0.5 msec, 1-20 sec). Vagus nerve stimulation induced a decrease in both frequency and amplitude of interictal spikes which outlasted the stimulus for up to 90 seconds. The threshold for suppression of respiration and heart rate by vagal stimulation was similar to that for an effect on cortical epileptiform activity (about 0.2 mA). A similar but less pronounced effect on spike activity was produced by placing the animal's tail in hot water for 40 seconds supporting the hypothesis that the effect of vagus nerve stimulation is mediated in a non-specific manner through the reticular activating system. In two animals which were stimulated at the onset of seizures, the seizure duration was decreased from a mean of 29 sec. without stimulation to a mean of 5 seconds. These findings provide some support for pursuing vagus nerve stimulation as a therapeutic alternative for the treatment of intractable epilepsy but raise some concerns regarding the safety of this procedure.

39.

The Impact of Out-Patient Video-EEG on the Detection and Characterization of Seizures in Childhood

M.B. CONNOLLY, K. FARRELL, Y. KARIM and P.K.H. WONG (Vancouver, British Columbia)

Video-EEG monitoring enables episodic behavioural events to be correlated with EEG activity. The usefulness of video-EEG in the evaluation of epilepsy patients for surgery and in the diagnosis of pseudoseizures is well recognized. However, the value of outpatient video-EEG in the management of children with minor motor seizures is less well recognized.

A 2-hour recording was obtained in 16 children (8 males), between 1 month and 13 years of age, using a sixteen-channel video-EEG. Most of the children had secondary generalized epilepsy, infantile spasms (6 patients), Lennox-Gastaut (3), severe myoclonic epilepsy of infancy (1), and atypical absence (2). The video-EEG was performed to determine whether the clinical event was an epileptic seizure (12 patients), the seizure type (3) and seizure frequency (1). The clinical events which were difficult to diagnose by history and inter-ictal EEG alone included subtle movements of the eyes (8), head nods (2), and minimal jerking of the limbs (3).

Clinical events were documented during video-EEG recording in 14 children. The investigation was unhelpful in two children in whom no clinical episodes occurred. Epileptic seizures were diagnosed in 12 children. One of two children in whom there was no electrical correlate with the clinical event developed generalized tonic-clonic seizures shortly after the study. The video-EEG permitted classification of the seizure type in 12 children. The seizure frequency was confirmed in one child.

Two hour video-EEG recording on out-patients is a useful method of studying children with frequent minor motor or subtle seizures, where there is a question regarding the nature of the episode, the classification of the seizure, or seizure frequency. This approach obviates the need for hospital admission with its associated economic and emotional cost.

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40.

The Use of SPECT with HMPAO Isotope for Identification of Focal Epileptic Activity

S.J. PURVES, W.B. WOODHURST, D.B. COUPLAND, B. LENTLE and M. WILSON-YOUNG (Vancouver, British Columbia)

99mTc-hexamethyl-propylene-amineoxime (HMPAO), single photon emission computed tomography (SPECT) has shown some promise in providing a non-invasive method to demonstrate focal cerebral hypoperfusion in the affected temporal lobe of patients assessed for surgical treatment of focal epilepsy. The importance of the timing of the post-ictal isotope injection and the relative sensitivity of interictal and post-ictal scans compared to CT and MRI remains uncertain.

In this study, 36 patients (19 with unilateral temporal epilepsy, 6 with focal extratemporal epilepsy and 11 with undetermined localization) had 55 HMPAO scans. 30 scans were done while the patient was on continuous 24-hour CCTV-EEG monitoring 10 to 38 minutes after an identified seizure. 25 scans were performed interictally.

In the 19 temporal lobe patients, 7/9 with abnormal MRI or CT scans and 8/10 with normal MRI and CT showed focal hypoperfusion on at least one HMPAO scan. There was a difference between interictal and post-ictal scans in all of the 12 patients who had both. Only 11/16 interictal scans were localizing. In the 11 patients with presumed extratemporal epilepsy, HMPAO-SPECT demonstrated focal hypoperfusion only in patients who had an identifiable structural lesion.

We conclude that 99mTc-HMPAO-SPECT Scans provides valuable lateralizing information for temporal lobe epilepsy and is most sensitive using a comparison between a post-ictal and interictal scan.

41.

Discovery of an Antiepileptic Peptide Through Computer Assisted Molecular Modelling Studies on the Voltage Regulated Sodium Channel Protein

D.F. WEAVER (Kingston, Ontario)

Although 1.5% of the general population experiences recurrent seizures, only 60-70% of these individuals enjoy reasonable control with currently available drugs. There is a need to design new and safer anti-convulsant drugs; in particular, there is a need to apply drug design techniques to the development of receptor site specific drugs with greater efficacy.

The 2,009 amino acid mammalian brain sodium channel protein has been computationally modelled using extensive molecular mechanics calculations. These modelling studies employed data from radio-labelling studies, neurotoxin mapping experiments and empirical predictions of protein secondary structure to facilitate calculational efficiency. These modelling experiments suggest that the protein consists of 4 domains each with transmembrane alpha helices interconnected by short beta turn segments. The modelling calculations were performed using large scale computing on RISC architecture computers.

This computer derived model of the voltage regulated sodium channel protein was then explored for potential drug docking sites capable of altering channel function. An appropriate site was identified consisting of a lipophilic pocket, two hydrogen bonding surfaces and an ionic surface. A conformationally constrained peptide capable of interacting with this site was designed and synthesized. This peptide has been called CDP15.

CDP15 has demonstrated significant anti-convulsant activity in the maximal electroshock test model. CDP15 has attained Stage VI in the 8 stage NIH Antiepileptic Drug Development Program. Preliminary biological evidence supports the sodium channel as the site of action of CDP15. More importantly, the activity of CDP15 is stereospecific being active in only one chiral configuration.

Therefore, CDP15 is an anticonvulsant peptide designed by large scale computational modelling.

42. Abstract Withdrawn

43.

Valproic Acid Suppresses Interictal Epileptiform Discharges in Patients with Primary Generalized Epilepsy. Phenytoin and Carbamazapine Do Not

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

Interictal epileptiform discharges are frequently used as objective support for the clinical diagnosis of epilepsy. Studies of the influence of antiepileptic medications on these EEG patterns, however, are few. We investigated the effect of 3 antiepileptic drugs on interictal epileptiform discharges in patients with primary generalized epilepsy.

Serial EEG tracings were obtained on 18 patients with primary generalized epilepsy who had been seizure-free for one year or longer on monotherapy with phenytoin (6), carbamazepine (5) or valproic acid (7). An additional 16 patients with new-onset seizures as a result of primary generalized epilepsy were similarly investigated.

EEG records obtained prior to the initiation of treatment demonstrated generalized bisynchronous spike and wave or multiple spike and wave discharges in all the patients. Serial follow-up EEG tracings of the 12 patients rendered seizure-free on phenytoin and carbamazepine continued to show the epileptiform abnormalities. In contrast, among the 23 patients treated with valproic acid, follow-up EEGs yielded no interictal epileptiform patterns in 18, all of whom remained without seizures. The EEGs of 3 patients who were also seizure-free demonstrated generalized multiple spike and wave discharges only during photic stimulation and the epileptiform activities did not outlast the procedure. Two patients continued to have seizures and their follow-up EEGs showed spontaneous and photic-induced generalized epileptiform discharges.

The differential effects of the antiepileptic drugs on interictal epileptiform patterns may relate to the differences in their mechanisms of action. Our observations suggest that in some patients with primary generalized epilepsy it may be possible to use the EEG as objective monitor of the response to treatment with valproic acid.

44.

Variability in the Clinical and Seizure Manifestations of Children with Occipital Paroxysmal Discharges

J. MAHER, G.M. RONEN, K.J. GOULDEN and A. OGUNYEMI (St. John's, Newfoundland)

In order to evaluate the specificity of the electrographic criteria for benign childhood epilepsy with occipital paroxysms (BCEOP),

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we reviewed the clinical state of all children whose electroencephalogram (EEG) was compatible with that diagnosis. Reports of all 5,291 EEGs done over 5 1/2 years in the only tertiary pediatric centre in Newfoundland and Labrador were reviewed. 80 EEGs from 43 patients were then read again by two electroencephalographers for the following EEG criteria (derived from a literature review of (B.C.E.O.P.).

(I) Normal background activity, with (II) focal epileptiform paroxysms in the occipital regions, uni- or bilateral, which are (III) partly or completely suppressed by eye opening.

Twenty-nine children fulfilled the criteria. Fifteen children had idiopathic partial epilepsy and a normal neurologic (including ophthalmologic) examination (B.C.E.O.P.). Nine had epilepsy and an abnormal neurologic examination. Three had only provoked seizures (1 with febrile convulsions, 1 with H. Influenza Meningitis, and 1 with severe anaemia). All 3 are now neurologically normal. Two patients were investigated for unusual nocturnal spells and had no definite seizures; both have cerebral palsy. Of the 11 children with an abnormal neurologic examination, 1 had Sturge-Weber Syndrome, 1 had Fetal Alcohol Syndrome, 1 had 4p-Syndrome, 7 had Cerebral Palsy and 1 patient had Cryptogenic Infantile Spasms with a poor outcome. Five of these had significant visual impairment.

In this EEG record based study, 38% (11 of 29) of children whose EEG fulfilled criteria for B.C.E.O.P. had significant neurologic impairment and a further 10% had only provoked seizures. The positive predictive value of these EEG criteria is 52%, therefore the accepted electrographic criteria for this benign clinical syndrome are not specific.

E. Neuromuscular

45.

Immunocompatibility for MHC Antigens of Class I and IIDr in Myoblast Transplantation for Duchenne Muscular Dystrophy

J.-P. BOUCHARD, R. ROY, J.P. TREMBLAY, J. HUARD and B. LEMIEUX (Sherbrooke, Québec, Québec)

Several investigators have shown that the normal gene for dystrophin could be introduced into dystrophic muscle fibres by injection of myoblasts from a normal muscle. We have obtained similar results in mdx mice. We then proposed to study whether such grafts were possible in Duchenne patients without using using immunosuppression. This had to be answered before the main hypothesis could be tested: does the graft of myoblasts improve strength or prevent weakness in boys with Duchenne and for how long?

All families with a boy alive and known as a Duchenne were contacted through three Muscular Dystrophy Clinics in Eastern Quebec. Information about the experimental nature of the study were given and 36 families enrolled in the study. Thirteen boys had a close relative compatible for MHC class I and IIDr. Eleven boys remained in the study, four in wheelchair and 7 still ambulatory. Three boys of 11, 13 and 16 years of age have received repeated injections of normal cultured myoblasts in the Tibialis anterior (TA) muscle of the left leg. There was no clinical sign of rejection (pain, swelling, fever). The presence of antibodies against the donor's myoblasts was tested by flowcytometry using the same clones of myoblasts kept in culture. In one patient antibodies were detected one month after the second injection. More studies are needed to understand the mechanisms of rejection in some cases and find the best way to alleviate them.

Muscle biopsies of the TA on both sides showed dystrophin positive muscle fibres in the injected side in the two patients free of antibodies. Six younger ambulatory patients are going to receive a graft in the biceps in a double-blind protocol without immunosuppression to verify the main hypothesis.

46.

X-Linked Muscular Dystrophy (X-MD) Diagnosed in Early Infancy

S.S. SESHIA, H. JACOBS, F.A. BOOTH, A. CAMERON, W. HALLIDAY, C. GREENBERG and K. WROGEMANN (Winnipeg, Manitoba)

X-MD can be diagnosed in the neonatal period by measuring creatine kinase (CK in the dried whole blood on filter paper. This method has been used to screen 45,000 newborn males prospectively from January 1, 1986 to December 31, 1990. Sixty had elevated levels, but the increase was persistent in only ten. In one, the elevation was in the CK-BB isoenzyme, while nine had CK-MM elevations. Of the latter, one, now deceased, had features of the Walker-Warburg Syndrome. The remaining 8 have X-MD and have been followed up in an unblinded manner for periods of 2 to 4 1/2 years. Their features are summarized:

(i) persistent and marked elevation of serum CK-MM in all, (ii) ultrasound examination of muscle abnormal in 1/5 by one year of age, (iii) EMG abnormal in 5/6, testing being done before muscle biopsy, (iv) muscle histology diagnostic of dystrophy in all, biopsies being done by one year of age in 6 and by 1 1/2 years of age in 2, (v) complete absence of dystrophin expression in all, predicting a Duchenne phenotype, (vi) with one exception, a normal examination until 12 to 18 months of age, (vii) development of calf hypertrophy, mild sternomastoid weakness and mild proximal lower limb weakness between 12 and 36 months of age, (viii) cardiac assessment normal in 4/4 and (ix) deletion or duplication in the dystrophin gene in 5/8.

One of the 8 is a familial case. The mothers of 4 of the remaining 7 have been identified as carriers.

The early diagnosis of X-MD is crucial for genetic counselling. In addition, the institution of treatment at an early age, is more likely to have a positive influence on the natural history of the disorder than treating such children when they are older.

Acknowledgement: CHWRF.

47.

Spectrum of Mitochondrial Encephalomyopathies

D. LAMOUREUX, K. SILVER, K. HODGKINSON, D. CHITAYAT and P. GOODYEAR (Montreal, Quebec)

Mitochondrial encephalomyopathies are a clinically heterogeneous group of diseases identified largely on the basis of morphological abnormalities of muscle mitochondria. Clinical recognition is difficult and it is likely that the number of cases are underestimated. We review the experience of the Montreal Children's Hospital. Twenty-two cases have been identified in the past 10 years.

The clinical, biochemical, radiological and pathological findings are reviewed. Four patients presented with defect of substrate utilization. The clinical presentation of each of these patients was different but they all have evidence of a defect of pyruvate

metabolism. Of special interest, is one of these patients presenting with cerebral dysgenesis, illustrating the prenatal effect of defect in energy metabolism on brain development. The rest of our patients can be classified under defect of the respiratory chain. Among them, five patients presented as Leigh Syndrome. Three patients presented with features consistent with MELAS Syndrome.

Cytochrome C oxidase represents the most frequent group. Five patients presented in the first months of life with a devastating encephalomyopathy. Three patients presented with features of a myopathic syndrome and two siblings presented with Menkes Kinky Hair Syndrome.

Our experience illustrates the heterogeneity of the clinical presentation and multi-organ involvement. There was poor correlation between phenotype and biochemical defect. A plan for non-invasive investigation prior to biopsy is proposed. It is emphasized that multiple types of evidence must be sought to document mitochondrial disorder, and the limitations of the different diagnostic tools are debated.

48.

Infantile Muscle Rigidity — An Ultrastructural Analysis

A.G. LACSON, J. HOOGSTRATTEN, W. DE GROOT, A. CHUDLEY, S.S. SESHIA, C. ADAMS and B. CHODIRKER (Winnipeg, Manitoba)

We have seen six cases of progressive early infantile muscular rigidity presenting with progressive respiratory distress, frequently complicated by secondary infection a few days to a few weeks after birth. The muscles characteristically become enlarged, firm and rubbery with enlargement of many muscle groups which tend to resist movement. Ventilator dependency sets in due to involvement of all respiratory muscles. Joint contractures and/or limitation of motion appear later. The reflexes remain normoactive. Creatine phosphokinase (CPK) levels are raised. All of our patients are native Indians from Northern Ontario. Three of the cases come from consanguineous unions. Muscle biopsies feature muscle fibre enlargement with focal and segmental granular transformation of the Z-bands, progressively involving the entire diameter of the fibre. The sarcomeres of adjacent myofibrillar bundles become out of phase; these changes differ from hypercontracted fibres where sarcoplasm details are lost. Actin predominate in later stages, with dense Z-band material and exclusion of thick fibres. Later the sarcoplasm is transformed into a large mass of amorphous densities, thin fibrils with glycogen particles and short whorls of thick fibrils. Many nuclei are large with nucleoli mimicking "regeneration". Full autopsy on one case disclosed no central nervous system abnormalities. Peripheral and intramuscular nerves are normal. Muscle spindles are prominent but normal. The finding of similar Z-band changes in an adult sporadic case of unclassified myopathy could indicate genetic heterogeneity or an acquired biochemical abnormality.

49.

Is Amyotrophic Lateral Sclerosis a Primary Disease of the Corticomotoneuron?

A. EISEN, B. PANT, S. KIM and C. KRIEGER (Vancouver, British Columbia)

Despite a century of study little is known about the interrelation between the upper and lower motor neuron in amyotrophic lateral sclerosis (ALS). It is widely assumed that both the corticomotoneuron (CM) and anterior horn cell (AHC) are involved independently. We, however, postulate that it is the CM that is initially involved; the AHC, with which it makes direct connection, is affected secondarily from antegrade effects. CM connections are sparse in nonprimates and our hypothesis explains the absence of animal models truly mimicking human ALS.

One indication of primary CM involvement is increased motor evoked potential (MEP) threshold to cortical magnetic stimulation recorded from a resting muscle of normal bulk and strength. Thenar and hypothenar muscle CM threshold measured in 20 normal subjects was 52.6 ± 5.7% and 57.3 ± 6.5% respectively. The difference reflects the greater thenar compared to hypothenar CM density. In 10 patients with ALS, having neither clinical or EMG evidence of lower motor neuron involvement of the tested hand, cortical threshold was significantly raised (mean = 78.4 ± 8.3%, $p > 0.001$).

Phylogenetically, corticomotoneuronal connections are unequalled in man allowing for highly fractionated movements. Unfortunately the trade off includes ALS.

50.

Seronegative Generalized Myasthenia Gravis: Low Frequency of Thymic Abnormalities

J. J-F OGER, P. VERMA and D. JELLEMA (Vancouver, British Columbia)

We have reviewed thymus histology, acetylcholine receptor antibody (AchR Ab) status and clinical presentation of all patients who underwent thymectomy for generalized myasthenia gravis since 1986 in UBC affiliated hospitals. Diagnostic criteria were clinical and electrical and included Tensilon® test.

Even though we have increased the sensitivity of AchR Ab detection (Oger, et al. Can J Neurol Sc 1987; 14: 297-302) and used human antigen derived from leg muscles at autopsy, we found that among 41 thymectomized patients 7 (14%) were seronegative. Of the 41 thymectomized, 24 (58%) had hyperplasia, 12 (29%) had normal thymus and 5 (12%) had thymona. The proportion of seronegative patients was greater among those with normal thymus (4/12, 33.3%) than those with thymic pathology (3/29, 10.9%). All of the 5 cases of thymoma had AchR Ab in their sera preoperatively.

Out of 11 sera (6 ocular and 5 generalized) which had tested negative with AchR isolated from human gastrocnemius, none tested positive using preparations made from human extraocular muscles, pharynx, tongue and diaphragm. Among GMGs, seronegative exhibited ocular and bulbar disease but minimal limb involvement. We conclude that among seronegative patients, one-half will have a pathologic thymus at surgery so the thymectomy remains indicated even if no antibodies are detected.

51.

Tremor Associated with Demyelinating Peripheral Neuropathy

T.W.J.W. WATSON, R.G.LEE and M. HULLIGER (Calgary, Alberta)

The association of tremor with peripheral neuropathy (PN) has been recognized since the early part of this century (Roussy and Levy Rev Neurol (Paris) 1926). Various hypotheses have been forwarded to explain the pathophysiology of tremor in the setting of

PN however the mechanisms involved remain unclear (Adams, et al. Trans Am Neurol 74; Said, et al. Neurol 82). We have studied two patients with PN associated with severe incapacitating tremor of the upper extremities.

Both patients were women whose symptoms developed in their early 50s. In each case the initial symptom was difficulty writing. Examination revealed areflexia in both upper and lower extremities. There was reduced light touch and vibration sense in a stocking and glove distribution with relative preservation of pain sensation. Surprisingly, position sense was normal and there was only mild $4^{+}/5$ weakness of intrinsic hand muscles. Both patients exhibited a coarse, slow (2-4 Hz) postural tremor of the hands and fingers accompanied by pronounced action tremor. Neither patient was capable of legible writing, drinking, or feeding themselves in a normal manner. There was no family history of PN in either case. Nerve conduction studies showed absence of sensory nerve action potentials and motor conduction velocities were severely reduced in the upper extremities (< 20 m/sec). Sural nerve biopsies showed chronic demyelination and extensive loss of large myelinated fibres. One patient had a polyclonal IgM gammopathy and in the other patient no specific cause was identified. Therapeutic trials of propranolol and primidone, and in one case VL thalamotomy, failed to alter the tremor.

The tremor will be demonstrated on video and discussion will focus on possible mechanisms underlying the production of tremor in PN.

52.

Intracellular Interactions in the Dorsal Root Ganglion Can Enhance Axonal Regeneration

X. LU and P.M. RICHARDSON (Montreal, Quebec)

Unknown responses of sensory neurons to peripheral nerve injury are known to contribute to axonal regeneration. To investigate the mechanisms by which these neuronal responses are initiated, regeneration of crushed axons in the fifth lumbar dorsal root of rats was assessed after putative enhancing stimuli to the dorsal root ganglion. The presence of isogenous macrophages injected into the ganglion or autogenous macrophages elicited by ganglionic injection of Corynebacterium parvum was shown to increase the number of regenerating fibres 17 days after dorsal root crushing. Sciatic nerve transection has been previously shown to have a similar enhancing effect. In examination of dorsal root ganglia after the sciatic nerve was cut, two cellular responses were observed. Proliferation of satellite glial cells was demonstrated by thymidine radioautography and infiltration of macrophages was detected by immunohistochemistry. The results indicate that the products of inflammatory cell can act in the vicinity of nerve cell bodies to enhance axonal regeneration. It is suggested that after peripheral nerve injury, non-neuronal cells in the dorsal root ganglion may participate in stimulating neuronal reactions that are beneficial to regeneration.

53.

Direct Muscle Neurotization of the Gastrocnemius Muscle as a Salvage Technique for Posterior Tibial Nerve Injury

J.A. MCLEAN, S. MACKINNON and G. HUNTER (North York; Toronto, Ontario)

The authors report the successful recovery of neurological function using a direct muscle neurotization technique.

A 39-year-old woman suffered a severe iatrogenic avulsion injury to the neurovascular bundle in the left popliteal fossa. Six weeks following a revascularization and fasciotomy procedure the avulsed posterior tibial nerve was reconstructed with nerve grafts (7 cables) from the proximal nerve directly into the distal gastrocnemius muscle. Sensory recovery to the foot was reconstructed transevering distal sural nerve into distal calcaneal and lateral plantar nerve.

Electrodiagnostics studies were performed preoperatively and at 30 months post-operatively. Preoperatively there was electrical evidence of denervation in the medial gastrocnemius muscle with minimal voluntary activity noted and marked improvement noted at 30 months.

Clinical examination demonstrated excellent functional recovery of gastrocnemius muscle function which has been sustained at 3 years of follow-up. Protective sensibility returned to the calcaneal and lateral plantar nerve distributions referable to the sural nerve distribution.

Conclusion: In the rare situation of avulsion of the distal portion of a critical motor nerve direct muscle neurotization should be considered. Although not previously described for the posterior tibial nerve this procedure offers the patient the possibility for potential functional recovery.

54.

Normal Hydrogen Clearance but Lowered Oxygen Tension in the Sciatic Nerve Endoneurium of Young Diabetic Animals

D.W. ZOCHODNE and LAM T. HO (Kingston, Ontario)

Studies of streptozotocin (STZ)-induced diabetic neuropathy (ESDN) at 4 months have identified endoneurial oligemia and hypoxia, but it is uncertain how early these abnormalities develop or which develops first. We studied ESDN in young (4 week) rats after 6 or 16 weeks of STZ-induced diabetes (or after citrate buffer injection in controls) by recording multifibre conduction in three different nerve territories and by measuring sciatic endoneurial blood flow (EBF) and oxygen tension ($Pn0_2$) at endpoint. EBF was measured using hydrogen clearance with an endoneurial microelectrode. Diabetes slowed the maturational increases in motor and sensory conduction and increased resistance to ischemic conduction failure. Despite this evidence of neuropathy, EBF was comparable to control animals at both time points and was within the published normal range. In contrast, the histogram of oxygen tensions was shifted to lower values in diabetic animals and mean $Pn0_2$ was lower at both time points. Our findings support the hypothesis that neuropathy occurs early in diabetes, but that hypoxia develops before endoneurial hydrogen clearance is slowed. The findings may suggest that oxygen carrying RBC transit failure (not assessed by hydrogen clearance) in the endoneurial microcirculation may be an early deficit in diabetic neuropathy.

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55.

Sustained Improvement of Inclusion Body Myositis with Prednisone and Azathioprine Treatment

W.K. ILSE, J.G. HUMPHREY and V. BRIL (Toronto, Ontario)

Inclusion Body Myositis (IBM) is an entity of undefined pathogenesis identified by specific pathologic stigmata, and characteristic clinical features. Resistance to immunosuppressive treatment has become accepted as a characteristic feature of the condition. Between January 1986, and December 1990 inclusive, IBM was diagnosed on 14 muscle biopsies at the Toronto General Hospital. Of the affected patients, two were followed elsewhere, and two were diagnosed recently. The remaining 10 patients, and one other with typical clinical findings, but non-diagnostic pathology, were followed for a mean of 31.8 months (9-54 months). The mean age was 60.5 years (31-76 years). There were 7 male and 4 female patients. Mean symptom duration at presentation was 3.7 years (1-7 years). Ten patients reported leg weakness, with difficulty in ambulation as the initial symptom. At presentation the upper and lower extremities were affected in, respectively, 6 and 10 patients. One patient complained of transient, mild dysphagia. On examination, the most consistent findings were weakness of the biceps, triceps, finger flexors, hip flexors, quadriceps,and ankle dorsiflexors. The degree of weakness was similar in all groups except the quadriceps, which was substantially weaker, and the ankle dorsiflexors, which were modestly affected. The serum Creatine Kinase was elevated in all patients, and all showed inflammatory myopathic changes on EMG. Oral azathioprine at 1.5 mg per kilogram and 50 mg of prednisone — tapered as permitted — were administered daily to all patients. In no case was treatment limited by any adverse reaction. All patients showed subjective, and objective improvement in strength within the first four months of treatment. Improvement was sustained in 9 of the 11 patients. Quadriceps improvement was twice that of most other groups. Finger flexors, and ankle dorsiflexors improved minimally. Serum CK showed a prompt, sustained decline.

In our experience, most patients with IBM achieve a sustained positive treatment response. We believe all patients deserve a therapeutic trial, as described.

FRIDAY, JUNE 21, 1991 – P.M.

F. Neurosurgery

56.

Intracranial Surgery in Patients with Cerebral Amyloid Angiopathy

R. LEBLANC, M. PREUL, Y. ROBITAILLE, J.-G. VILLEMURE and R. POKRUPA (Montreal, Quebec)

In cerebral amyloid angiopathy (CAA) the contractile elements of leptomeningeal and cortical arteries are replaced by non-contractile amyloid material. CAA is seen with advancing age, senile dementia of the Alzheimer type (SDAT) and spontaneous cerebral hemorrhage (ICH). Multiple ICHs separated in time and space are frequent, and post-operative hemorrhage can follow cortical surgery. Previous studies have been autopsy-based and may be biased towards a poor prognosis for ICH from CAA. We have reviewed 19 patients with CAA in whom surgery was performed. Surgery was elective in 8 patients who underwent cortical biopsy for diagnosis of SDAT without resultant hemorrhage. A second group of 11 patients had acute or delayed surgery for ICH from CAA, 4 with the misdiagnosis of hemorrhage within a tumour. Three patients, in poor neurological condition at the time of surgery, died from the initial ICH or from the complications of debilitation. Four survived with a severe neurological deficit or organic brain syndrome and 4 others, operated on in good neurological condition in a delayed fashion, were well at the time of discharge. Two patients who survived the initial surgery had repeated hemorrhages. This was fatal in one case and aggravated a neurological deficit in the other.

The role of surgery in patients with CAA is being delineated. Our study suggests that cortical surgery in the absence of an ICH can be accomplished safely if meticulous attention is given to hemostasis. Delayed surgery in ICH-patients in good neurological condition is sometimes well tolerated and acute surgery in patients in poor neurological condition is associated with high mortality and morbidity.

57.

Neurogenic Pulmonary Oedema Associated with Subarachnoid Hemorrhage

M. BOJANOWSKI, A. BOUTHILLIER, J.G. GUIMOND and C. JOLY (Montreal, Quebec)

Neurogenic pulmonary oedema (NPO) may occur following subarachnoid hemorrhage (SAH). Beside being potentially responsible for cerebral hypoxia, it may prevent the institution of volume expansion in patients at risk of cerebral vasospasm.

During 1987-1990, nineteen cases of NPO were encountered. This group is compared to other patients with SAH but without NPO (96 patients) seen in the same period. Fifty-three percent of patients with NPO were in a severe clinical grade at admission (Hunt and Hess grade 4 and 5). Loss of consciousness (100%) and convulsions (53%) at the onset of SAH were important risk factors. Seventy-nine percent of the patients with NPO developed cardiac abnormalities. The majority of NPO (68%) was established within 24 hours after SAH.

Most of these patients (84%) were in radiological grade 3 (Miller-Fisher). Hydrocephaly and ventricular inondation were significantly more frequent in the NPO group. These patients had more medially situated aneurysms and the anterior cerebral artery was always involved when vasospasm was present. The chest X-rays showed perihilar distention and pleural effusion associated with NPO in 74% and 44% respectively. The PCWP values were frequently near the upper limit of normality. Calcium antagonists did not contribute to produce NPO. There was no mortality directly related to NPO. The incidence of brain infarction was not increased in the NPO group.

This study suggests that NPO is much more frequent than previously thought. Some characteristics are better defined. With the current treatment of invasive monitoring, NPO did not increase the mortality nor the incidence of brain infarction.

58.

Polycystic Kidney Disease and Cerebral Aneurysm: Is There a Genetic Link?

A. LOZANO and R. LEBLANC (Montreal, Quebec)

Adult polycystic kidney disease (APKD) is an autosomal dominant, inherited disorder in which up to 40% of patients may have an

intracranial aneurysm. The pathogenic basis of this association is unknown. We have compared cerebral aneurysms in patients with APKD to the sporadic aneurysm cases reported by the Cooperative Study to determine if there are significant biological differences between these two groups. One hundred reports of patients with aneurysmal subarachnoid hemorrhage and APKD were screened. Of these the patients' age, sex and site of rupture were available in 79 cases. Sixty-eight patients had a single aneurysm and 11 (14%) had multiple aneurysms. In APKD patients with subarachnoid hemorrhage from a single aneurysm there was a significant over-representation of males (72%, $p < 0.01$); and the APKD group had more aneurysms of the middle cerebral artery (37%, $p < 0.05$) and fewer of the internal carotid artery (18%, $p < 0.05$). The peak decennial incidence and mean age of rupture of APKD-associated aneurysms was younger (mean age 39.7 years, $p < 0.01$) and over 77% of APKD-associated aneurysms had ruptured by age 50 versus 42% for sporadic aneurysms ($p < 0.001$). Cerebral aneurysms co-existed with APKD in the absence of hypertension in 26.6% of 45 cases where the presence or absence of hypertension was recorded.

The biological differences of APKD-associated aneurysms and their occurrence in normotensive APKD patients suggests an etiology which may be independent of hypertension and that APKD-associated aneurysms may be genetically determined. It is hypothesized that cases of inherited, familial cerebral aneurysms could be linked to a genetic defect resembling that which occurs on chromosome 16 in APKD, a hypothesis testable with current genetic-probing techniques.

59.

Predicting Functional Recovery After Surgical Treatment of Chronic Subdural Hematomas By Multivariate Analysis of Presenting Clinical Parameters

S. BRIEN and W.J. HOWES (Halifax, Nova Scotia)

In 150 patients with chronic subdural hematomas, several presenting clinical parameters were subject to multivariate analysis and the usefulness of this statistical method in predicting the functional recovery was evaluated. Variables such as blood pressure, bilaterality, CT density, presence of blood on CT scan, midline shift, presenting neurological grade and mode of surgical management were assessed to further delineate that subpopulation of patients who require more than one surgical procedure.

A numerical prediction of functional recovery was derived from an equation in which each variable was scored and weighed. This value was compared with the actual functional recovery grade (Glasgow Recovery Scale).

Functional recovery can be extrapolated from presenting clinical data.

60.

Surgical Versus Non-Surgical Treatment of Neonatal Intraventricular Hemorrhage

F.W. GAMACHE and M. BILSKY (New York, U.S.A.)

Charts of 130 neonates treated non-surgically for neonatal intraventricular hemorrhage were randomly chosen for review for the treatment period 1984-1989. 68 of the 130 babies had hemorrhage outside the ventricle as well. 79 of 130 were judged radiographically to have mild or moderate hydrocephalus (none severe). 118 babies experienced respiratory distress syndrome. Cardiac abnormalities, sepsis, necrotizing enterocolitis were frequently encountered. A history of maternal drug abuse during pregnancy was elicited in 10% of cases. Seizures occurred in 1/4 of the babies. 77 babies were available for follow-up evaluation: 32 were developmentally normal, 45 were abnormal. There were 26 deaths due in decreasing frequency to refractory cardiac problems, pulmonary failure, sepsis, multi systems failure.

During the same time interval 54 babies were treated with ventricular diversion procedures for intraventricular hemorrhage. Mean gestation, Apgar score, birth weight were not significantly different than the above group. 25 had extra ventricular hemorrhage as well. Hydrocephalus was judged radiographically as severe in 22 babies. Following the initial ventricular diversion procedure 41 babies underwent a single, 11 a second, and 3 a third revision. 19 of the 25 shunt obstructions were associated with recent ventriculitis/peritonitis. 60 percent of shunted babies experienced seizures. On follow-up of 40 babies 8 were judged as normal, 32 as abnormal. 11 deaths occurred (4-39 weeks) post-operatively: generally because of refractory cardiopulmonary failure.

61.

Skull Remodelling After Sagittal Synostosis Repair

M. MATISHAK, D. COCHRANE and P. STEINBOK (Vancouver, British Columbia)

Many different operative procedures have been advocated for the repair of sagittal synostosis. The importance of operating early in life has been stressed on the premise that the skull continues to expand, resulting in a gradual return to a more normal shape over time.

Head circumference, maximum length and maximum width of the cranium were measured preoperatively and sequentially after surgery in 34 patients with sagittal synostosis. The horizontal cephalic index i.e.: the width/length (HCI) was used to monitor progression of skull remodelling. All patients were operated on prior to 18 months of age using a variety of surgical procedures based on intraoperative findings and the preference of the surgeon.

Maximal skull reshaping as measured by the greatest change in HCI occurred within the first two months post-operatively. This pattern of change was noted irrespective of age at operation or the type of procedure performed. The HCI then stabilized or decreased though never to baseline values.

Contrary to what is generally believed, further normalization of head shape as measured by the HCI does not appear to occur more than 2 months after surgical correction of sagittal synostosis in infants.

62.

Craniocervical Fusion with Contoured Luque Rod and Autogeneic Bone Graft

P.M. ELLIS and J.M. FINDLAY (Edmonton, Alberta)

A technique of craniocervical fusion useful for severe instability is presented.

We have used this method to fuse three patients with craniocervical instability from diverse causes. The first patient was a rare case of survival after traumatic atlanto-occipital dislocation. The second case, with congenital occipitalization of the atlas, demon-

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strated a progressive post-laminectomy swan neck deformity and basilar invagination. The third patient had odontoid erosion and swan neck deformity from severe rheumatoid disease and presented with progressive quadriparesis from an intraspinal pannus.

A contoured Luque rod was wired to the subocciput and all affected cervical levels. The first case had sublaminar wiring. The third patient required a decompressive laminectomy, and along with the second patient had the rod wired to the facet joints. In all cases, instrumentation was followed by autogeneic iliac grafting with morcellated cancellous bone. The second patient was kept in a halo brace for four months post-operatively and the others were maintained for the same time in a Philadelphia collar. All patients stabilized or improved neurologically and follow-up x-rays demonstrated reduction in deformity with solid bony fusion.

The technique is simple and provides immediate and absolute fixation in cases of severe instability and obviates adjunctive external stabilization in most cases.

63.

Juxta-Apophyseal Cysts

A.L. AMACHER (Danville, U.S.A.)

Cystic space-taking lesions arising from or intimately associated with the apophyseal joints may cause spinal radicular or stenotic syndromes. Preoperative recognition of this pathology is facilitated by routine spinal MRI or CT scanning. Contrast myelography is of little value in preoperative diagnosis. In that percutaneous CT-guided puncture and drainage of a symptomatic cyst is a feasible therapeutic option, accurate preoperative diagnosis has relevance.

In consecutive series of 1,525 lumbar and 320 cervical procedures for relief of radicular or stenotic symptoms during the interval 1986-1990, 14 lumbar and 1 cervical juxta-apophyseal ("synovial") cysts were encountered, an incidence of 0.8% for lumbar and cervical sites. This presentation will describe typical clinical and radiologic criteria for diagnosis and discuss treatment options.

64.

Dynamic Stereotactic Radiosurgery: Measured Accuracy and Clinical Results

M.L. SCHWARTZ, P. O'BRIEN, C. YOUNG and P. DAVEY (Toronto, Ontario)

The Sunnybrook/Toronto Bayview Regional Cancer Centre Linear Accelerator Radiosurgery Unit has treated 20 patients since its inception 27 months ago. Podgorsak's dynamic technique of simultaneous couch and gantry rotation with certain modifications[1] is utilized. Ten patients who had received conventional, external beam whole brain radiation for metastases but who relapsed, have so far been treated with a typical prescription of 25 Gy at the isocentre. Ten patients with arteriovenous malformations measuring less than 3 cm in diameter have also been treated with a typical dose of 25 Gy at the isocentre prescribing a maximum dose of 15 Gy to critical structures at the perimeter of the lesion.

Using an anthropomorphic phantom, the accuracy of dose delivery at the isocentre was confirmed with measurements both ionometrically for large fields and with thermo-luminescent detectors (TLD) for small fields. The disk-shaped TLD's were arrayed in stacks in drill holes in the phantom symmetrically placed with respect to a central aluminium target. The target was localized by means of CT scanning and then irradiated. In 3 independent experiments, the measurements agreed with predicted dose values to within 1 percent. Spatial accuracy was measured with the TLD arrays for the x, y and z stereotactic coordinates. The average combined error in localization was 0.93 mm. This compares with accuracy estimates for radiosurgery units using multiple collimated stationary radioactive sources (Gamma knife).

There have been no acute clinical complications so far. The growth of individual metastases so treated has been arrested. Follow-up on the earliest treated arteriovenous malformations is now becoming available and will be discussed.

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[1] O'Brien PF, Gillies BA, Schwartz M, Young C, Davey P. Radiosurgery with Unflattened 6MV Photon Beams. Medical Physics (accepted for publication).

65.

Complications Following Dynamic Stereotactic Radiosurgery: Review of 112 Patients

J-.L. CARON, M.R. MCKENZIE, L. SOUHAMI, A. OLIVIER, J-G. VILLEMURE and E.B. PODGORSAK (Montreal, Quebec)

Between December 1986 and June 1990, 112 patients were treated with dynamic stereotactic radiosurgery at McGill University. There were 62 females and 50 males, ranging in age from 5 to 59 years (median 35 years). Of treated lesions, 57 were arteriovenous malformations (AVM), 11 cavernous angiomas, 11 brain metastasis, 11 gliomas, and 22 a variety of other neoplastic and non-neoplastic conditions. All patients were treated with only one isocenter and the target volume was assumed spherical. The dose was prescribed at the 90% isodose surface. In 81 patients, treatment was delivered in a single fraction, ranging from 15 to 50 Gy (median 36 Gy), with field sizes ranging from 5 to 30 mm in diameter (median 10 mm). In the remaining 31 patients, treatment was fractionated with the prescribed dose ranging from 21 to 50 Gy (median 42 Gy), in 2 to 10 fractions (median 6 fractions), with field sizes ranging from 10 to 30 mm in diameter (median 20 mm).

Early toxicity was seen in 3 patients. One developed transient homonymous hemianopsia within a few hours of treatment; a few weeks following radiosurgery, another patient developed markedly increased seizure activity which did not respond to treatment. Within weeks following irradiation, the third patient developed increased hemifacial weakness which ultimately resolved. Four suffered late toxicity. Three of them developed vasogenic edema at 6, 11, and 14 months following irradiation. Two of them responded to steroids and recovered completely and one failed to respond to steroids, later dying of intracerebral hemorrhage from her AVM. In the fourth patient, brain necrosis developed 6 months after treatment. In this group of patients, there appeared to be no relationship between complications and total dose, fractionation, field sizes, or site of the lesion treated. An updated analysis will be presented.

66.

Retrospective Evaluation of 246 Patients Having a Chronic Pain and Treated by Electrical Neurostimulation

S.N. MARTINEZ, P. MOLINA NEGRO, M. GLYNN and D. RENE (Montreal, Quebec)

From May '79 to December '90, more than 15,000 patients suffering from chronic pain with multiple etiologies have been investi-

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gated at the Pain Centre of Notre-Dame Hospital. Various therapeutic orientations have been used according to the pathology.

The multidisciplinary group, mostly made up of neurologists, neurophysiologists, neurosurgeons, psychologists and psychiatrists, has selected 246 patients for electrical neurostimulation.

The surgical techniques were spinal cord stimulation (SCS) for peripheral pain syndrome (arachnoiditis, minor causalgia, peripheral vascular disease, etc.) and deep brain stimulation for deafferentated pain (anesthesia dolorosa, thalamic syndrome, brachial plexus avulsion and painful phantom limb).

Short and long term results for each pathology treated plus the solution of inherent problems to the surgery and the material used will be presented.

G. Cerebrovascular

67.

Clinical Stroke Scales — Which One to Use?

M. HOHOL and S.E. BLACK (Toronto, Ontario)

For therapeutic trials in acute stroke reproducible and valid methods of quantifying neurologic deficit are essential, yet no consensus exists as to the best clinical stroke scale. In an ongoing longitudinal study of stroke recovery three widely used stroke scales were compared: Canadian Neurological Scale (CNS) (Cote R, et al., 1986) NIH Stroke Scale (NIH) (Brott T, et al., 1989) and Hemispheric Stroke Scale (HSS) (Adams R J, et al.,1987). Scores were expressed as a percentage with higher values reflecting greater severity.

For non-comatose patients (N = 58) mean scores in the first week were: HSS 40, NIH 33 and CNS 38 ($p < 0.0001$). At one month (N = 25) all scales showed a significant change in mean scores ($p < 0.001$), with an average improvement of 7%. There was no significant difference in percent improvement ($p = 0.8$).

By design, all patients can be fully assessed on the CNS, whereas the percent of non-assessable items in the first week was 16% on the NIH and 18% on the HSS (48% in severe strokes). Non-assessable items were rated as a maximal deficit. At one month, these figures improved to 6% for the NIH and 7% for the HSS.

Given these preliminary results we found the Canadian Neurological Scale the most useful in the early phase of stroke. It is brief and simple with good inter-rater validity and can be administered by a nurse or physician.

However, for milder strokes and for follow-up of specific deficits, the HSS or NIH are more informative. This may be important in assessing longer term functional outcome after therapeutic intervention.

68.

Carotid Stenosis and Ischemic Stroke

C.Z. ZHU, A. PIRISI and J.W. NORRIS (Toronto, Ontario)

Most ischemic strokes are due to carotid stenosis or cardioembolism, but a large minority remains unexplained ("cryptogenic strokes"). To elucidate this problem further, we compared the data from our stroke register to the carotid Doppler laboratory data in consecutive patients admitted to the Stroke Unit.

Of 360 patients, there were 15% (54) with vertebrobasilar ischemic events, and 10% (36) with cerebral hemorrhagic events. 75% (270) had carotid ischemic events, and of these, 27 had TIAs, leaving 243 patients with carotid ischemic strokes, of whom 25% (61) had neck bruits and 75% (182) did not. In 9% of patients, carotid Doppler could not be performed. In carotid stroke patients with neck bruits, 85% (52) had carotid stenosis but only 30% (55) without neck bruits had carotid lesions; i.e., in only 44% (107) could carotid stenosis explain their strokes.

Only a minority of carotid ischemic strokes are associated with carotid artery stenosis. The "cryptogenic" majority remains unexplained.

69.

NMDA-Receptor Antagonist Drugs May Have Widespread Effects in Ischemia

S. TAKIZAWA, M.J. HOGAN, A. GJEDDE and A.M. HAKIM (Montreal, Quebec)

We evaluated the kinetic and physiologic properties of CGS-19755, a competitive blocker of the NMDA-receptor reported to have protective effects in ischemia.

By quantitative in-vitro autoradiography in normal rats we showed the regional distribution of ^{3}H-CGS-19755 to be proportional to the selective vulnerability of the regions in ischemia. Occlusion of the left middle cerebral artery (MCA) and common carotid artery (CCA) four hours prior to autoradiography did not affect this binding, indicating that only maximum activation of the NMDA receptor may be measurable by this technique.

We then measured the rate of transfer of this drug into the brain. In normal rats the regional plasma clearance across the blood brain barrier was very low, averaging 0.015 ml-100g^{-1}-min^{-1}. In rats with prior MCA + CCA occlusion this clearance value averaged 0.019 ml-100g^{-1}-min^{-1} in the ischemic hemisphere, and 0.09 ml-100g^{-1}-min^{-1}.in the non-ischemic hemisphere, indicating that ischemia does not substantially increase this drug's transport into brain.

Finally, we determined cerebral blood flow (CBF) and pH (CpH) simultaneously 4 hours after MCA + CCA occlusion in rats which received this drug immediately after occlusion and compared them to controls. In the ischemic caudate and cortex CBF (mean±SEM) went from 8 ± 3 and 21 ± 4 respectively in carrier controls to 27 ± 16 and 63 ± 1 3 ml/100g/min in CGS-19755-treated rats. The acidosis accompanying the ischemia was also improved. Thus, while CGS-19755 seems to bind approximately to the vulnerable brain region, its rate of transfer into the brain is likely too small to make its therapeutic effectiveness dependent on its NMDA blockade. Rather, its powerful vasodilator effect may be a significant factor.

Supported by MRC, NIH, Ciba-Geigy Canada

70.

Nimodipine Binding in a Reversible Model of Focal Cerebral Ischemia

M.J. HOGAN and A.M. HAKIM (Montreal, Quebec)

Activation of neuronal cell membrane calcium channels is an early metabolic consequence of severe cerebral ischemia. In-vivo binding to brain of the 1,4-dihydropyridine calcium channel antagonist, nimodipine, is increased in ischemia. This binding is saturable and specific to the L-type voltage sensitive calcium channel and may be used as an indicator of channel activation and thus identify

neurons at risk of suffering ischemic injury. To explore if early ischemic activation of the calcium channels is reversible we have assessed nimodipine binding in a model of reversible focal cerebral ischemia.

Focal cerebral ischemia was produced by combined occlusion of the middle cerebral artery and ipsilateral common carotid artery by micro-aneurysm clips in rats. Nimodipine binding was assessed autoradiographically using [^{3}H]-nimodipine administered 30 minutes prior to decapitation of the rats. Binding was assessed after 15 minutes of focal ischemia and after 45 minutes of recirculation following 15 minutes of focal ischemia.

Nimodipine binding was increased in both ischemic striatum and cortex. Increased binding in the ischemic cortex decreased to levels comparable to binding in the non-ischemic hemisphere cortex while increased binding in the caudate showed only a partial decline following 45 minutes of recirculation. Histology studies performed at 24 hours showed infarction in the lateral aspect of the ischemic striatum.

These results demonstrate that calcium channel activation occurs within minutes of the onset of cerebral ischemia but is initially reversible. This reversibility is only partial in severely ischemic regions that progress to infarction despite restoration of blood flow but is nearly complete elsewhere. Therefore this response may be a useful model to assess the effectiveness of potential future therapies for cerebral ischemia.

Supported by MRC, HSFC, and Miles Laboratories.

71.

The Use of In-vitro Binding with 3H-Forskolin as an Ischemia Marker following Experimental Middle Cerebral Artery Occlusion

M.C. WALLACE and I. DARAMOLA (Toronto, Ontario)

Reliable identification of cellular changes following the onset of focal ischemia is difficult up to four hours after middle cerebral artery occlusion (MCAO). Clearly, important pathophysiology occurs during this interval and a cellular marker for ischemia would be a valuable investigation tool. This report describes the use of in-vitro binding with 3H-forskolin, a ligand for the cAMP second messenger system, after MCAO in the rat.

Adult Fischer 344 rats (n = 20) underwent general anaesthesia with 1% Halothane and nitrous oxide:oxygen. Animals underwent middle cerebral artery occlusion (n = 17) or sham procedure (n = 3). Temperature, blood pressure and arterial blood gases were controlled. Animals were sacrificed at 30 minutes (n = 5), 1 hour (n = 4), 2 hours (n = 4) or 6 hours (n = 7) following MCAO. In-vitro binding with 3H-forskolin, was carried out on 20μm brain sections and quantitative autoradiography was performed. Histological analysis was performed on each animal.

Infarction was identified by histology at 6 hours but not at earlier time periods. 3H-forskolin binding in the ischemic caudate at 3 hours post MCAO was 39 ± 1 pmoles/gm, relative to 104 ± 9 in the contralateral caudate nucleus ($p < 0.01$). Cortical binding was also reduced by 22% at 2 hours and remained depressed at 6 hours post MCAO ($p < 0.05$). The loss of 3H-forskolin binding at 6 hours post MCAO correlated by region with the histological identification of infarction.

3H-forskolin binding is markedly decreased following focal cerebral ischemia. This decrease can be recognized prior to available pathological outcome measures for cerebral ischemia. This methodology will be a valuable tool for the investigation of cerebral ischemia, particularly in the evaluation of cerebroprotective agents in focal ischemia.

72.

Dynamic Transcranial Doppler Waveforms and Autoregulation

R.L. BONDAR, R. AASLID, M.S. KASSAM, F. STEIN and P.T. DUNPHY (Toronto, Ontario; Berne, Switzerland)

Transcranial Doppler (TCD) measures blood flow velocities noninvasively in the basal cerebral arteries. Clinically, static measurements of these velocities can indicate vasospasm, for example, in subarachnoid hemorrhage. The actual waveform, however, is a reflection of both upstream circulatory dynamics and downstream autoregulatory changes in addition to local vessel diameter alterations.

To assess the contribution of upstream forces on the TCD signal, 10 healthy subjects were exposed to reproducible transient changes in acceleration force, including microgravity, by means of parabolic flight in NASA's KC-135 aircraft. Continuous arterial blood pressure (Finapres ABP), acceleration and TCD recordings of the right middle cerebral artery, were monitored and recorded simultaneously on digital audio tape (DAT) for off-line analysis. Data was recorded over five 75-second parabolas, with the subject in the supine position.

The dynamics of the maximum TCD frequency waveform and the corresponding ABP for each cardiac cycle were analyzed with respect to changes in acceleration force. Significant changes in both ABP and TCD waveforms were observed, particularly during the transition phases of the acceleration profile. In addition, these results also lend themselves to analysis of autoregulation mechanisms through modelling.

73.

Spontaneous Dissections of the Basilar Artery

S.P. LOWNIE, A.J. FOX and C.G. DRAKE (London, Ontario)

Over the past 15 years, 8 cases of spontaneous dissection of the basilar artery have been encountered at the University of Western Ontario. Two of these were bland dissections, presenting with brainstem and/or cerebral infarction. One died and 1 survived. Six patients presented with subarachnoid hemorrhage (SAH) due to a dissecting aneurysm. Three survived and 3 died.

Review of the cases of bland dissection, in combination with cases from the literature, yielded a total of 15 cases. The patients were young (average age 32 years), usually male (73%), and most had a poor outcome. Those presenting with SAH (a total of 10 cases including the literature) also tended to be young (mean age 43 years), but were more often female (80%), and tended to have predisposing conditions such as hypertension, diabetes or a history of smoking. Of the patients with SAH, rebleeding occurred in only 1 case. Overall survival was related to the presence of absence of brainstem infarction, the length of the dissection, and the tendency for rebleeding. The difference in the sex distribution between hemorrhagic versus bland dissections was statistically significant ($0.025 < p < 0.05$).

74.

Endovascular Therapy of Non-Galenic Cerebral Arteriovenous Fistulae

S.P. LOWNIE, G.R. DUCKWILER, A.J. FOX and C.G. DRAKE (London, Ontario; Los Angeles, U.S.A.)

Cerebral arteriovenous fistulae not involving the vein of Galen are uncommon lesions. In the combined experience of the University of Western Ontario and the University of California at Los Angeles, 13 cases have been encountered, of which 10 were treated. Five were treated surgically by proximal occlusion of the feeding artery(ies), with excellent results in 4 and 1 death. Two of these patients had failed an endovascular approach. Four patients were treated using endovascular methods with excellent results in 3 and 1 death. One patient was treated with a combined approach with an excellent outcome. The results were similar to a review of cases encountered in the literature (excellent or good results in 23 of 26 treated patients).

Cerebral arteriovenous fistulae not involving the vein of Galen are clinically distinct from vein of Galen aneurysms. Two-thirds of the patients presented over the age of two, and the clinical presentation was related to mass effect in two-thirds and seizures in one-third. The natural history of these fistulae appears to be related to the number of major arterial territories supplying the varix.

Endovascular therapy has evolved as the preferred initial approach, with surgery as a generally fail-safe alternative.

75.

Seizures after Stroke

A. PIRISI, C.Z. ZHU, S.E. BLACK, J.A.G. McLEAN and J.W. NORRIS (Toronto, Ontario)

The relevance of seizures following stroke, to management and prognosis remains uncertain and poorly documented.

We prospectively evaluated 898 patients with acute stroke over a period of one month to 5 years. 128 with brainstem strokes had no seizures. 79/770 (10%) with hemispheric lesions had seizures, of these 44% occurred on the first day, 63% in the first week and 87% in the first year. The incidence of seizures in hemorrhage and infarction was the same.

Cerebral lesions in the seizure group were twice the volume (on CT) than the non-seizure group (52 cm^3 compared to 26 cm^3). Seizures were more frequent in embolic (30/70) compared to non-embolic (176/621 strokes ($p < 0.04$). Mortality was higher in the seizure group ($p < 0.02$).

Seizures in acute stroke occur predominantly in the first week, are more frequent in embolic stroke and confer a poor prognosis.

76.

Mannitol Accumulation in Vasogenic Cerebral Edema: An Experimental Study in Cats

A.M. KAUFMANN and E.R. CARDOSO (Winnipeg, Manitoba)

The cerebral accumulation of mannitol and associated changes of cerebral water content and edema progression were assessed in a feline vasogenic edema model ($n = 23$). Treatment groups received either one or five doses, q4h, of 0.33 g/kg^{-1} radiolabelled mannitol. Mannitol concentrations were measured by liquid scintillation counting.

There was no accumulation of mannitol in plasma. Mannitol did however accumulate in the cerebral tissue. The concentration in non-edematous white matter following a single dose was 0.028 ± 0.002 mg/g. Following five mannitol infusions, the concentration increased three-fold to 0.102 ± 0.010 mg/g. The concentration of mannitol in the edematous white matter was 0.193 ± 0.016 mg/g following a single dose. After five doses the concentration was 0.331 ± 0.032 mg/g, and exceeded trough plasma levels by a ratio of 3.0. This concentration gradient across the blood-brain barrier would favour the flux of water into the brain. In fact, mannitol treatment did not reduce the linear progression of edema, nor was cerebral water content reduced four hours following a single dose. However, following repeated infusions of mannitol, edematous cerebral water content **increased** to $86.3 \pm 0.5\%$, compared to $83.3 \pm 0.2\%$ in controls ($p = 0.0034$). This potential to exacerbate cerebral edema with repeated mannitol doses might outweigh therapeutic benefits in patients with vasogenic cerebral edema.

77.

The Investigations of Unexplained Intracerebral Hematomas: The Role of MRI and Delayed Angiography

R.A. WILLINSKY, P. FITZGERALD, W. MONTANERA, K. TERBRUGGE and C. WALLACE (Toronto, Ontario)

Based on a retrospective review of 16 patients with cerebral micro arteriovenous malformations (AVMs) (< 1 cm) an imaging algorithm for the investigation of unexplained intracerebral hematomas (ICH) can be proposed. There were 13 men and 3 women with a mean age of 40 years. Eleven of the patients presented with an ICH. Eleven patients had MRI and a vascular abnormality was evident in 5. Angiography established the diagnosis of a micro AVM in all cases. In 3 patients, initial angiography was negative, but follow-up angiography six weeks or later showed the malformation.

We propose the following approach to unexplained ICHs. After CT establishes the presence of an ICH, angiography should be done. A micro AVM or other vascular etiology may be found. If the initial angiogram is negative a baseline MRI may reveal an underlying mass or suggest a cavernoma. If the cause for the ICH is still not clear a follow-up MRI at 6-8 weeks is recommended. At this time the hematoma will have resolved and the presence of a cavernoma may be clear. If a hemosiderin cleft is seen then a follow-up angiogram should be done.

A search for micro AVMs in the face of an ICH is important since they are treatable and can remain undiagnosed. Often the only clue of their presence is an early vein on angiography. Repeat angiography may be necessary. We feel that most of the so called "angiographically occult" malformations are either micro AVMs or cavernomas.

H. Neuro-oncology

78.

Management of Intracranial Midline Low Grade Astrocytomas in Children

H.J. HOFFMAN, D. SOLONIUK, R.P. HUMPHREYS, J.M. DRAKE, E.B. HENDRICK and L. BECKER (Toronto, Ontario)

The authors have reviewed the results of management of intracranial midline low grade astrocytomas treated at The Hospital

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for Sick Children during the years January 1976 to December 31, 1990. During this period, 88 patients consisting of 52 boys and 36 girls ranging in age between 2 months and 17 years were treated for intracranial midline low grade astrocytomas. The 88 tumours consisted of 43 optic pathways and hypothalamus tumours, 13 thalamic tumours, 6 pineal tumours, 15 midbrain tumours, and 11 medullary tumours. Among the 88 patients, 33 had pilocytic tumours and 55 had fibrillary tumours. Seven patients with pilocytic tumours have died (mortality rate 21.2%) and 2 of the 55 patients with fibrillary tumours have died (mortality 3.6%). Among the 35 patients who were treated with radiotherapy initially, 15 had recurrences, 4 had tumour dedifferentiation into an anaplastic astrocytoma, 8 have significant hypopituitarism and 9 have a significant intellectual deficit. With radiotherapy some of these low grade tumours will disappear, others will stabilize and some will continue to grow. Direct surgery can be carried out on these midline low grade astrocytomas in childhood without significant morbidity or mortality. Many of these patients will do well with resection as the only form of therapy with the residual tumour involuting after resection without any other form of therapy.

79.

Detection and Management of Intracranial Gangliogliomas in Children: Particularly with Temporal Lobectomy

H. OTSUBO, H.J. HOFFMAN, R.P. HUMPHREYS, E.B. HENDRICK, J.M. DRAKE, P.A. HWANG, L.E. BECKER and C. NETLEY (Toronto, Ontario)

Thirty-three children treated at The Hospital for Sick Children, Toronto, for intracranial gangliogliomas, were reviewed to identify the best methods of detection and management. Of these tumours, 29 were supratentorial including 16 in the temporal lobe, and 4 were infratentorial. Patients included 23 males and 10 females. In the 16 patients with temporal gangliogliomas, males predominated, with a male-to-female ratio of 13:3. Twenty-three patients presented with seizures, with a mean duration of symptoms of 5 years, in contrast to 1 year in non-seizure patients. Of 26 children studied with CT scan, calcification in the tumour lesion was found in 18. All patients underwent surgical resection and were diagnosed pathologically. Twenty-two patients had total resection of their tumours, and 12 patients underwent anterior temporal lobectomies with hippocampal excision, which revealed mesial temporal sclerosis in 6 of 12. Nine of 12 patients with the temporal lobectomy were free of seizures for a follow-up period of 6 months to 9 years. We suggest that children with long-standing complex partial seizures be studied with CT scan and MRI, which would detect the ganglioglioma and/or mesial temporal abnormalities correlating with epileptogenic foci in electrophysiological studies. They require removal of the epileptogenic lesion as well as the ganglioglioma.

80.

Quality of Life in Long-term Survivors of Cerebellar Medulloblastoma

R. HOLNESS, W. HOWES, G. MURRAY, D. LOUW and J. PADILLA (Halifax, Nova Scotia)

Thirty-four children with histologically proven cerebellar medulloblastomas were encountered in Halifax during a 25 year period. One patient presented in extremis, and one died post-operatively. Thirty-two patients were treated with radical tumour removal followed by radiation therapy. Six also received adjuvant chemotherapy as part of the CCSG and RTOG study. Complications of surgery caused mild, compensated neurological deficits in 5 and 3 required long-term shunts.

We report a follow-up assessment of the quality of life experienced by 10 disease-free, long-term survivors. Three patients have survived for more than 20 years. Four patients are disease-free at 10-15 years and 3 have survived from 5-10 years. Two survivors with evidence of recurrent disease were excluded from this analysis.

By routine examination 9 of the 10 patients are normal, or near normal (Bloom's class I-II). One patient is totally disabled (Class IV). We also examined intellectual and endocrine outcomes. Five patients have growth hormone deficiency. Two of these have severe pan hypopituitarism and evidence of hypothalamic dysfunction. Apart from the totally disabled patient, 3 others have mild learning disabilities and 1 a mild behavioral disorder. All others are intellectually normal. The 3 long-term survivors who received combination radiotherapy and chemotherapy have the worse deficits in intellect, endocrine and neurologic function. The most severely disabled is in this group and was treated at age 2.5 years. The others were treated at 3.7 and 9 years of age respectively. The least affected of these 3 had been treated with low dose radiotherapy (3500 rads).

Poor outcomes show a relationship to the dose of radiation therapy and whether chemotherapy was used. The combination of age <5 years with post-operative radiotherapy with maximal levels and adjuvant chemotherapy seems particularly unfavorable. So far we have not encountered recurrent medulloblastoma or radiation induced neoplasms in patients who have survived >8 years.

81.

Peptic Ulcer Disease in Children Receiving Dexamethasone for Palliation of Progressive Brain Tumours

C.B. VAN ORMAN and H.M. MACHIDA (Calgary, Alberta)

Brain tumours are the second most common form of cancer in childhood. Gastrointestinal (GI) manifestations are common and generally are attributable to raised intracranial pressure and tumour infiltration into the floor of the fourth ventricle. It is well recognized that stress ulcers, presenting with vomiting, hematemesis and abdominal pain, may occur in the immediate post-operative period. New or worsening GI symptoms that subsequently arise usually indicate continued tumour growth or hydrocephalus. Corticosteroids are efficacious in reducing tumour associated edema but their use has been associated with peptic ulcer disease in adults. We report 6 children (ages 3-14 years), with primary brain tumours — medulloblastoma (2), brainstem glioma (2), thalamic glioma, fourth ventricular ependymoma — and progressive disease despite conventional treatment, who developed GI symptoms which included at least two of the following: anorexia, abdominal pain, persistent vomiting, hematemesis and epigastric tenderness. Five of the patients were taking dexamethasone at the time the symptoms began. All patients had significant improvement in their symptomatology following anti-peptic ulcer disease therapy. In one case, an upper GI series demonstrated complete obstruction of the distal antrum or pylorus, which resolved with intravenous ranitidine. The other 5 patients were treated empirically with benefit. Peptic ulcer disease must be considered as a potential cause of GI symptoms in children receiving corticosteroids for pallitation of primary brain tumours. The use of peptic ulcer disease prophylaxis needs to be evaluated in this population.

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82.

In Vivo Measurement of Blood-Brain Barrier Permeability in Human Brain Tumours with X-Ray Computed Tomography

R.F. DEL MAESTRO, W.T. I. YEUNG, T-Y LEE, R. KOZAK and T. BROWN (London, Ontario)

A method has been developed to measure the in vivo cerebral plasma volume (V_p) and the forward transfer constant (K) of iopamidol in brain tumour patients using a clinical x-ray CT scanner. In these studies, Isovue 300 was injected at a dosage of 1 ml/kg patient body weight. Serial CT scans of the tumour site and arterial blood samples from the same radial artery were taken up to 48 minutes after injection. The leakage of iopamidol into the brain through the blood-brain barrier was modelled as an exchange process between two compartments, the intravascular plasma space and the tissue interstitial space. Using this model and the concentration measurements in blood plasma and tissue, quantitative estimates of K and V_p in brain tumours were obtained. In addition, distribution of the estimated values of K and V_p were displayed as false colour functional images overlaid on the conventional CT scan.

In this study of thirteen patients with anaplastic astrocytoma (n = 3), glioblastoma multiforme (n = 4), metastases (n = 5) or meningioma (n = 1), the mean K and V_p values in tumour were found to be 0.0275 ± 0.0053 ml/min/g and 0.075 ± 0.012 ml/g respectively. These values were significantly higher than those in normal grey or white matter ($p < 0.05$). The functional images showed variations in K and V_p within the tumour which were difficult to perceive in the original contrast enhanced CT scans.

83.

Correlation of Magnetic Resonance Images with the Histopathology of Interstitial Laser Photocoagulation in Brain

S.W. SCHATZ, D.R. WYMAN, R.A. TRACZ, P.B. LITTLE and B.C. WILSON (Hamilton; Guelph, Ontario)

Interstitial delivery of low power laser energy can produce controlled, thermal destruction of normal brain or tumour. To assess the feasibility of monitoring the spatial and temporal evolution of effective tissue necrosis, we have studied the T1- and T2- weighted magnetic resonance (MR) images of proton density in cat brain – in vivo – before, during and after Nd: YAG laser illumination at 1064 nm via an optical fibre inserted into parietal lobe. The diameter of the fibre was 400 microns; its end was plane-cut. Continuous wave output powers of 1.0, 1.5 and 2.0 watts for periods of 1000 seconds, gave total energy deposition of 1000, 1500 or 2000 joules respectively. The MR images were correlated with the changes seen on immediate histo-pathological examination, or were repeated prior to histo-pathological examination after 48 hours. T2- weighted images (T2w) acquired during illumination have better contrast than T1-weighted images (T1w) but following illumination, Gadolinium enhanced T1w images are similar to T2w images. T2w images acquired during illumination have a well defined dark region of signal loss. On T2w images after exposure the dark area has a bright centre and is surrounded by a bright halo. The latter is more prominent at 48 hours and appears to extend into the white matter of both hemispheres of the brain. The diameter of the lesions in tissue or image measured 10-11 mm acutely, and somewhat more (12-13 mm) with the reaction developing in the 48 hours after exposure. Bright MR signals appear to represent fluid or edema. The dark area corresponds to an area of obvious coagulation necrosis surrounded by tissue which appears to be non-viable but the extent of permanent, irreversible damage will be assessed in animals surviving for longer periods following laser exposure. We are experimenting with rapid imaging techniques to permit monitoring of laser photocoagulation as it would develop during treatment of a brain tumour.

84.

The Role of Transsphenoidal Surgery in the Treatment of Craniopharyngiomas

M. PARE, J. HARDY and P. BOURGOUIN (Montreal, Quebec)

A retrospective review of the clinical features, perioperative course and postoperative outcome was effected in 60 patients with craniopharyngiomas treated surgically by the senior author (J.H.) between 1963 and 1990. There were 30 men and 30 women ranging in age from six to 66 years. Children under the age of 20 composed 38% of this group. Endocrine deficits preoperatively were present in 43% of patients. The most common presentation was growth failure in children (51%) and sexual dysfunction in adults (22%). 52% presented with visual deficits. Forty patients were treated by transsphenoidal surgery. Thirty-eight of these patients had an enlarged sella; 31 had a suprasellar extension. Nine patients had a large intrasphenoidal expansion. Two patients with normal sella (Grade I) were also operated by T.S. Twenty patients with suprasellar tumor and normal sella were operated by intracranial (I.C.) approach.

In the T.S. group, removal of the tumour and its capsule was considered complete in 30%, partial in 28% and the capsule was left intact in 42%. In the I.C. group, radical removal was possible in 62% and partial removal in 38%.

There were no operative mortality. In the T.S. group, endocrine function was improved in 36% of patients with preoperative deficits, unchanged in 24% and worsened in 40%. Visual deficits were improved in 32%, unchanged in 60% and worsened in 8%. In the I.C. group, endocrine improvement was seen in 10% and worsening was observed in 35%.

Follow-up of patients ranged between one and 28 years. There were eight recurrences in the T.S. group (20%) and three in the I.C. group (15%). Reoperation was performed in ten cases. Worsening of the patient condition at reoperation occurred in two of the T.S. group and all of the I.C. group. Three patients received radiotherapy.

These results suggests that transsphenoidal surgery is the preferential approach to craniopharyngiomas in patients with an enlarged sella turcica even with a large suprasellar expansion. It is less traumatic, associated with less postoperative endocrine deficits and less visual complications. Recurrences after incomplete removal is also amenable by T.S. approach with less complications than by I.C. approach.

85.

Oncocytoma and Oncocytic Changes in a Large Series of Pituitary Adenomas

M.C. Preul, S. Marcovitz, J. Hardy and W. Duguid (Montreal, Quebec)

Pituitary oncocytomas were first described in 1973. The significance and natural history of oncocytomas and corresponding oncocytic changes in pituitary adenomas have not yet been elucidated.

We reviewed 505 pituitary adenomas which were resected by transsphenoidal craniectomy at our institution between 1975 and 1990 and examined by light and electron microscopy. There were 43 cases (20 males, 23 females) of oncocytoma and oncocytic changes. The mean age of males was 56 (range 35-82) and females 40 (ranged 18-59) years. There were 17 frank oncocytomas: 11 non-secreting [NS] (mean size 2.0 cm in diameter); 4 prolactin-secreting [PRL] (1.2 cm); 2 growth hormone-secreting [GH] (2.9 cm). Oncocytic changes were noted in 14 PRL adenomas: 7 marked (1.2 cm), 6 moderate (0.9 cm), 1 mild (0.7 cm); in 8 GH adenomas: 4 marked (1.2 cm), 4 moderate (1.6 cm); in 3 ACTH adenomas: 2 moderate (0.6 cm), 1 mild (1.0 cm). Oncocytic tumours were 8% of 505 adenomas; 5% of 67 ACTH adenomas; 20% of 54 NS adenomas; 7% of 258 PRL adenomas; 8% of 124 GH adenomas. Our series shows that oncocytic changes occur in a continuum of severity; there seems to be an association of more marked changes with increasing tumour size. Many adenomas display features of oncocytic changes without being characterized as oncocytomas. The clinical course of patients was variable: one had documented evidence of rapid tumour growth over 3 years followed by recurrence after surgery requiring reoperation and radiotherapy; another had a tumour which invaded dura and nasopharyngeal mucosa; a third with a large tumour had complete recovery of pre-existing endocrine deficits and remains free from recurrence 7 years after operation.

86.

Large Pituitary Adenomas: Clinical Presentation and Complications of Surgical Treatment

P.J. MULLER, A. GUHA and K. WILLIAMS (Toronto, Ontario)

We reviewed 106 patients with pituitary adenomas who came to surgical treatment at St. Michael's Hospital, Toronto, over an 8 year interval.

There were 14 microadenomas [<1 cm diameter], all of whom presented with an endocrine disturbance. The male/female ratio 2/12 [0.16] and the mean age was 36 ± 12 years. All underwent a transsphenoidal adenectomy. There were no deaths and the only complication was transient diabetes insipidus [DI].

There were 42 macroadenomas [up to 2.5 cm diameter, filling the sella with or without a suprasellar extension (SSE)]. The male/female ratio was 24/18 [1.33] and the mean age was 46 ± 15. SSE occurred in 28/42 and sphenoid invasion in 4/42. An endocrine presentation occurred in 26/42 and visual presentation in 12/42. All but 2 had transsphenoidal surgery. Eleven had transient DI and 3 had complications [1 infection + CSF leak, 1 CSF leak and 1 fatal pulmonary embolus]. Operative mortality rate was 2%.

There were 50 large pituitary adenomas [>2.5 cm, all with SSE]. Fifteen of these cases had tumours >4 cm. Sixteen were null cell adenomas, 14 oncocytomas, 10 prolactinomas, 2 corticotroph adenomas, 2 silent corticotrophs and 2 gonadotroph cell tumours. Three presented with neurological deficit, 4 with endocrine symptoms and 43 with visual symptoms. The male/female ratio was 34/16 [2.13] and the mean age was 53 ± 16. Transsphenoidal resection was carried out in 28 and transcranial resection in 22. Serious complications were noted in 10 cases. There was sellar hemorrhage in 5 [3 of these were fatal], infection in 3, CSF leak in 2 and seizures in 2. A further 2 patients in this series died >2 years after initial treatment [one from lung cancer and one from delayed meningitis]. The operative mortality was 6% and non-fatal complication rate was 14%.

Large and giant pituitary tumours tend to present with visual symptoms, have a male preponderance, occur in older patients than their smaller counterparts and tend not to be endrocrinologically active. These tumours continue to be a neurosurgical challenge.

87.

Brain Tumours and Pregnancy

G. HADDAD, F. HADDAD, K. WORSELEY and J.-G. VILLEMURE (Montreal, Quebec; Beyruth, Lebanon)

Numerous reports have linked CNS neoplasms to pregnancy. Our objective was to answer the following questions: 1) Are CNS neoplasms more prevalent in pregnant women as compared to an aged-matched non pregnant control group? 2) Does pregnancy exacerbate the symptoms of CNS neoplasms?

1) All meningiomas, schwannomas, glioblastomas multiforme, astrocytomas grade 2, hemangioblastomas and oligodendrogliomas operated at the M.N.H. between 1960 and 1985 were reviewed (1,329 cases). Of these, 16 occurred in pregnant women. The observed/expected ratios were calculated for each tumour and ranged from 1.19 for schwannomas to 3.17 for hemangioblastomas. These differences were not statistically significant.

2) 107 meningiomas operated in Lebanon between 1955 and 1980 as compared to 48 gliomas operated during the same period. All the patients were married, non-widowed women in the child-bearing age (15-45 years). The percentage of pregnant women was 25.2% and 20.8% for the meningioma and glioma groups respectively. Upon studying the emergence and evolution of symptoms in these two groups, it became apparent that in the meningioma group symptoms appeared predominantly before (30.4%) or during pregnancy (65.2%), whereas in the glioma group symptoms appeared during pregnancy (50%) or in the puerperdum (30%). The meningioma group was further characterized by an abrupt worsening of symptoms during pregnancy and a definite improvement in-between multiple pregnancies. This pattern was not observed in the glioma group.

88.

The Management of Malignant Astrocytomas by Computer-Guided Stereotactic Biopsy and Radiation

M. WEST and D. FEWER (Winnipeg, Manitoba)

We prospectively studied the management of 31 malignant astrocytomas which were diagnosed by computer-guided stereotactic biopsy using the BRW frame. 66% of the patients were males. The mean age was 58 years. Five patients were excluded from analysis because they (a) had subsequent tumour resection (2), (b) presented with recurrent tumour (2), or (c) belonged to the pediatric population (1). Of the 26 patients remaining, 7 patients and/or their families declined postoperative radiation because of poor quality of life (due usually to severe aphasia associated with a dominant hemisphere lesion, or dementia associated with a lesion of the corpus callosum). Nineteen patients with Grade 3 and 4 astrocytomas were treated with radiation (average 5,000 cGy). 70% of the tumours were deep within the cerebral hemispheres. 70% were in the left hemisphere and 12% were located in the midline. Hemorrhage at the time of biopsy caused a clinical deterioration in 1 patient. There were no infections and no deaths. Patients were discharged within 2 days of biopsy. The median survival for patients who did not under-

go radiation was 12 weeks. The median survival for those treated with radiation was 35 weeks. This figure compares favorably with the median survival of 40 weeks recorded historically for patients with glioblastoma multiforme treated by surgical excision and post-operative radiation. Our experience suggests that the results of treatment of malignant astrocytomas by stereotactic biopsy and radiation is comparable to the results obtained by surgical excision and radiation. This may reflect a possible earlier presentation of the more sensitively located lesions comprising this series. Stereotactic biopsy followed by radiation is an acceptable efficacious treatment of the patient with malignant astrocytoma, especially when the tumour is located in an area which precludes uncomplicated surgical excision.

89.

Effect of Acetylsalicylic Acid on Radiation Brain Damage in a Rat Brachytherapy Model

M. BERNSTEIN, J. GLEN, K. PARSONS, O.A.M. ZERDONER and J. STEVENS (Toronto, Ontario)

Interstitial brachytherapy with high activity removable radiation sources is currently under study for patients with malignant brain tumours. An important and perhaps dose limited complication of brachytherapy is radiation toxicity – seen early as cerebral edema or late as so called radiation necrosis. Numerous pharmacological agents may attenuate radiation damage and acetylsalicylic acid (ASA) was selected for its anti-platelet properties which may result in reduction of the vascular component of radiation injury.

A model to study radiation brain damage in a rat brachytherapy model was recently established (J Neurosurg 1990; 73: 585-593). In the current study 30 rats were divided into three groups of 10 each. Each group received interstitial radiation with an Iodine-125 seed laid on the cerebrum to deliver a dose of 80Gy to a point 5.5 millimetres from the midpoint of the seed. Group I received no additional treatment. Group II received low dose ASA (10mg/kg) administered by orogastric gavage daily starting one week prior to irradiation, no treatment during the radiation period, daily for one month following seed removal, and then on weekdays for the remaining 5 months. Group III rats received high dose ASA (50mg/kg) by the same route and timing as the low dose group. Six months following irradiation the animal were studied with gadolinium enhanced MRI (two millimetre thick coronal slices). The MRI slices demonstrating abnormal uptake of gadolinium were loaded into a computerized image analysis system for 3-dimensional volumetric reconstruction.

Mean volumes of radiation injury (ie. gadolinium enhanced MRI lesion) were 83.9, 76.9 and 45.5 cubic millimetres for groups I, II and II respectively. There were no statistically significant differences between groups (one-way analysis of variance). In other words ASA appeared not to reduce radiation damage in a rat brain brachytherapy model.

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I. General Neurology

90.

Intravenous Gammaglobulin in Acute Inflammatory Polyneuropathy (Guillain-Barre Syndrome): Three Case Reports.

R.K.B. PEARCE, J.G. HUMPHREY, V. BRIL (Toronto, Ontario)

The efficacy of intravenous human gammaglobulin is well documented in chronic inflammatory demyelinating polyneurpathy (CIDP), but its use has not been well described in acute inflammatory demyelinating polyneuropathy (Guillain-Barre Syndrome, GBS). We report three patients with severe GBS refractory to conventional therapy with plasmapheresis and immunosuppression, who responded to gammaglobulin therapy.

Two patients had acute, relapsing GBS with recurrent episodes of weakness evolving rapidly over hours to days, requiring repeated intubation and ventilation in one patient. Both patients had a temporary response to plasmapheresis. One patient suffered multiple line-related complications and those of chronic steroid administration. With gammaglobulin therapy, administered every 4-5 weeks, this patient tolerated the tapering of immunosuppressive medication and did not require further plasmapheresis. This patient's strength returned to normal. In the second patient a single course of gammaglobulin therapy induced a prolonged remission. A third patient with monophasic GBS progressing in spite of plasmapheresis improved after gammaglobulin infusion.

Intravenous gammaglobulin is a safe therapy which may be effective in the Guillain-Barre Syndrome when plasmapheresis fails.

91.

Intrathecal Baclofen for Treatment of Spasticity in Children: Report of 9 cases

P. STEINBOK, R. ARMSTRONG, K. FARRELL, A. REINER and D. COCHRANE (Vancouver, British Columbia)

Intrathecal baclofen as a method of treatment for spasticity was studied in nine children with spastic quadriplegia related to cerebral palsy(4), cervical cord injury(2), head injury(2), and near drowning(1). A subcutaneously placed access device, was attached to a catheter inserted into the lumbar subarachnoid space at L3-4. Daily baclofen boluses were given in increasing doses, until the maximum relief of spasticity occurred or side effects were observed. A double blind assessment was then determined using the most effective dose of baclofen versus saline as placebo.

Eight patients had a beneficial response to the intermittent doses of baclofen. In these children the access device was replaced with a pump to allow continuous infusion of intrathecal baclofen. The children have been followed from six months to three years after insertion of the pump, with daily baclofen doses of 250 ug to 1000 ug.

With the use of intrathecal baclofen, spasticity was reduced, more in the lower than upper limbs, spasms were eliminated, and improvements were noted with respect to ease of care, seating and behaviour. There were no significant central nervous system side effects with the appropriate doses of baclofen. There were some mechanical complications affecting delivery of the drug, and one meningitis associated with the access device.

The study suggests that continuous intrathecal baclofen may be a useful therapeutic modality in the management of children with spastic quadriplegia.

92.

Selective Functional Posterior Rhizotomies for Spastic Cerebral Palsy: Experience with 50 Cases

P. STEINBOK, R. BEAUCHAMP, A. REINER and D. COCHRANE (Vancouver, British Columbia)

50 consecutive children are described with spastic cerebral palsy treated with selective bilateral functional posterior rhizotomies of the L2 to S1 or S2 roots from February 1987 to June 1990. All patients were followed for at least six months. The age at surgery ranged from 2.2 years to 18.1 years. 28 children were diplegic, 21 quadriplegic and 1 triplegic.

In all patients, spasticity improved dramatically in the lower limbs immediately after surgery. In 39 patients improvements were noted at levels of the central nervous system above the lumbar segments. All 17 children who could walk pre-operatively could walk following rhizotomies, and in 15 gait was improved. 18 children who could not walk prior to surgery were able to walk with a walker post-operatively. Complications included transient urinary dysfunction in four children, and an intraoperative spinal subdural hematoma in one patient.

The operative procedure evolved with time: the technique of replacement laminotomy was refined; the electrophysiologic basics for selection of nerve rootlets changed; there has been a trend toward preservation of a large part of the nerve roots involved with quadriceps function, and toward sectioning a smaller percentage of each nerve root.

The data suggest that selective functional posterior rhizotomies may be useful in the management of selected children with spastic cerebral palsy.

93.

An Unusual Case of Acute Lead Encephalopathy in a Six-Week-Old Infant

M.B. CONNOLLY, E.H,. ROLAND, G. LOCKITCH, L. WADSWORTH and F. MIRHADY (Vancouver, British Columbia)

Exposure to lead in childhood may result in anemia, neurological abnormalities and growth failure. We report an unusual case of acute lead poisoning in a six-week-old infant whose only oral intake was breastmilk and infant formula.

The patient was a six-week-old female who was hospitalized for sudden onset of several left-sided focal motor seizures which lasted approximately 10 minutes and were controlled with phenobarbital.

The birth history and family history were unremarkable. The child had received only breastmilk and commercial formula.

On examination, the infant was irritable. The head circumference was 40 cm (+2SD). The anterior fontanelle was soft. Cranial nerve examination was normal. There was increased muscle tone and hyperreflexia. The general physical examination was normal.

There was a normocytic, normochromic anemia (hemoglobin 66 g/L) with stippled erythrocytes. Bone marrow examination demonstrated erythroid hyperplasia and dyserythropoiesis. The white blood cell and platelet counts, serum iron level, transferrin and ferritin were normal. Cranial CT and ultrasound scans were normal. The EEG was abnormal with suppressed background and multifocal sharp waves. Cerebrospinal fluid examination was bloodstained: bacterial and viral cultures were normal. The blood lead level was 7.45 µmol/L (normal < 0.72 µmol/L). Erythrocyte protoporphyrin was 13.2 µmol/L (0.18 - 1 µmol/l)/ X-Rays of the long bones demonstrated lead lines.

The source of the lead was an electrical urn of Iranian origin which had been bought at a local store and which was used to boil water for preparation of formula. The concentration of lead in water boiled in the pot was 54-84.94 µmol/L, which is 350 times greater that the Canadian standard for drinking water.

The infant received chelation therapy and had no further seizures. Her development and EEG are normal at one year of age.

Lead poisoning was initially considered unlikely because of the young age and because feeding was limited to breastmilk and commercial formula. This case emphasizes the importance of searching for unusual sources of lead poisoning in infants who present with seizures and anemia.

94.

Migraine and Mitral Valve Prolapse: Related Conditions or Chance Association? A Controlled Study Using the New Classification of the International Headache Society

R. DESBIENS, C. ROBERGE, S. DESBIENS, D. SIMARD, C. NADEAU and G,. HOUDE (Montréal; Québec, Québec)

Although migraine is a very common disorder, its cause is still unknown and no biologic marker has been identified. Numerous studies reported an association between migraine and mitral valve prolapse (MVP), but few of those used controls or blinded investigators. In addition, the diagnosis of migraine was always based on the 1962 definition of migraine rather than on the more precise criteria devised in 1988 by the International Headache Society.

Our study compares the prevalence of MVP in a group of migraineurs and in a headache-free control group. Migraineurs were referred by neurologists. Controls were matched for age and sex and denied having headaches. A total of 192 patients and controls were interviewed and examined using a strict protocol. Echocardiography and auscultation were performed by a cardiologist blinded for the neurologic diagnosis, using standard techniques and diagnostic criteria for MVP. Each exam was kept on videotape and was reevaluated by another cardiologist. Thirty-three subjects were excluded: 13 were non migraineurs, 11 controls had tension-type headache, 9 had equivocal or uninterpretable echo. One hundred and five migraineurs (38 with and 67 without aura) and 54 controls were included in the study. Nine (8.6%) MVP were found in the migraine group and 2 (3.7%) in the control group. The difference between the two groups is not significant.

Previous studies have reported MVP in 14-37% of migraineurs and in 7-15% of controls. Although our methods are similar to those used in most studies (except for the diagnostic criteria of migraine), and although the ratio of the percentages of MVP in migraineurs vs controls is 2.3, no statistically significant association could be demonstrated.

Our results suggest that there is no clinically significant association between migraine and MVP when strict criteria are used to diagnose both disorders.

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95.

An Unusual Cluster of Four Cases of Severe Encephalomyelitis with Favorable Outcome

T.J. MARRIE, R.A. PURDY, C.W. McCORMICK, B.L. JOHNSTON and L.P. HEFFERNAN (Halifax, Nova Scotia)

Between March 19, 1990 and July 25, 1990 we studied 4 patients, age range 18 to 35 years with encephalomyelitis. All had a 6 to 14 day prodrome of upper respiratory tract symptoms followed by a progressive neurological illness starting with low back pain followed by urinary retention, leg weakness, diminished or absent sensation, alteration of consciousness, cranial and/or peripheral nerve palsies. the most severely affected individual developed quadriparesis, hypothalamic dysfunction and respiratory failure. All 4 had CSF pleocytosis — 82-100% mononuclear cells. All 4 patients were treated high dose corticosteroids for 10 days — three recovered full neurological function within 2 months, 1 still has nocturnal urinary incontinence at 6 months and has optic neuropathy in the right eye secondary to the severe papilloedema that accompanied her acute illness. Extensive microbiological investigations have shown only elevated (1:32 to 1:64) stable antibody titres to adenovirus. Specifically Lyme and arbovirus titres were negative. In a previous study of 338 adults with community-acquired pneumonia we found the 319 (94%) had no detectable antibody to adenovirus; only 1 had an antibody titre of 1:32, 11 had an antibody titre of 1:16. There was no geographic clustering but the temporal association of 4 cases of this illness suggests an infectious or more likely a parainfectious etiology. The high degree of recovery is unusual for such a severe illness.

96.

Reductions of Thiamine-Dependent Enzymes in Frontal and Temporal Cortex in Alzheimer's Disease

R.F. BUTTERWORTH (Montreal, Quebec)

Previous studies suggest that alterations of thiamine-dependent enzymes may play a role in the deficit of cognitive function in Alzheimer's Disease. Autopsied brain tissue (frontal and temporal cortex) was obtained from 6 patients with neuropathologically confirmed Alzheimer's Disease, from equal numbers of patients who died in hepatic coma resulting from alcoholic cirrhosis and from control subjects free from neurological, psychiatric or metabolic diseases. Thiamine-dependent enzymes (pyruvate dehydrogenase (PDHC), α-ketoglutarate dehydrogenase (αKGDH) and transketolase (TK) as well as glutamate dehydrogenase (GDH) and choline acetyltransferase (CAT) were measured in brain homogenates. PDHC activities were reduced by 70% ($p < 0.01$), αKGDH activities reduced by 71% ($p < 0.01$) in both temporal and frontal cortex of Alzheimer's patients when compared to alcoholics or control subjects. Brain tissue from both Alzheimer's patients and alcoholics contained significantly reduced activities of TK. GDH activities were normal in brain tissue from both Alzheimer's patients and alcoholics. CAT activities were significantly reduced (by 41%, $p < 0.01$) in Alzheimers brain tissue in parallel with the loss of activities of thiamine-dependent enzymes. CAT activities in the brains of alcoholics were within normal ranges. Selective loss of PDHC and αKGDH with concomitant loss of cholinergic integrity could be responsible for the cognitive defects encountered in Alzheimer's Disease. [Funded by MRC Canada]

97.

The Treatment of Catatonia with Lorazepam: A Study of 26 Cases

P.I. ROSEBUSH, M.F. MAZUREK, A. HILDEBRAND and G. GAIND (Hamilton, Ontario)

Following up on case studies, we have recently reported that the catatonic syndrome may respond dramatically to lorazepam. Since our original report we have had the opportunity to study an additional 11 episodes of catatonia, bringing the total to 26. A diagnosis of catatonia was made if four or more of the following were present: immobility, staring, mutism, rigidity, withdrawal, posturing/grimacing, negativism, waxy flexibility, echolalia, echopraxia, stereotypy and verbigeration. CT examination was performed in 22 and EEG in 14. Each patient was given lorazepam 1-2 mgs po/IM, re-evaluated at hourly intervals and questioned when no longer mute, about the subjective sense of anxiety during the catatonic episode. In 19 cases, all of whom had a purely "retarded" type of catatonia, there was a dramatic resolution of the syndrome within two hours. Each of these patients looked terrified and each reported experiencing intense anxiety during the episode. Four of the 19 had an identifiable organic contribution to their catatonia. A partial response was observed in an additional 3 patients. Of the remaining 4 patients who had no response to lorazepam 3 had "psychogenic" catatonia characterized by periods of marked excitement while the fourth had normal pressure hydrocephalus requiring neurosurgical intervention. Conclusions: (1) lorazepam produces a rapid and dramatic resolution of clinical signs in most cases of catatonia; (2) the response to lorazepam may not be a useful indicator of whether the catatonia is of organic or psychogenic etiology; (3) low-dose lorazepam may be more effective in treating catatonia of the purely "retarded" as opposed to the "excited" type; (4) the response to lorazepam was correlated with the presence of anxiety, suggesting that its efficacy in catatonia may be related to its anxiolytic properties.

98.

Quantitation of Two-Finger Tapping, Clinical Usefulness and Validation of a Simple Bedside Test

B. GIMBARZEVSKY and D. PARTON (Vancouver; Prince George, British Columbia)

Qualitative evaluation of finger tapping (ftap) has been used clinically as a test of fine motor function. We have recently investigated the clinical utility of this test by obtaining quantitative measures of finger tapping performance utilizing a computerized data acquisition system of our own construction. Our preliminary work has revealed this test to be a sensitive and reproducible measure of fine motor function. As quantitative data is obtained, this test has considerable potential utility in following progression of patients with neurologic disease affecting fine motor function and their response to treatment.

From 45 control subjects (SS) tested, following 8 parameters were calculated: S1(R), S1(L), mean tapping interval for right and left hands, S2(R), S2(L) mean intervals in 2 finger tapping, S2/S1 for each hand and S1(R)/S1(L), S2(R)/S2(L). Confidence limits were established for each parameter and a scoring algorithm was developed which allowed clear separation of SS's with neurological disease from controls. This scoring algorithm as well as normal

ranges will be presented. There was no notable effect of age on ftap parameters. Males were found to be non-significantly faster than females in tapping rates so data from both sexes were combined for construction of limits of normalcy.

A total of 7 SS's with neurologic disease (3 Parkinsons, 1 progressive supranuclear palsy, 1 motor neuron disease, 1 old stroke, 1 severe peripheral nerve disease) were tested. In these SS's one or more of the following abnormalities were found: (1) very prolonged tapping intervals, (2) increased differences between left and right hands, (3) normal S1 but abnormally long S2 times (this also gave increased S2/S1). This latter pattern was seen in all Parkinsonian SS's tested.

99.

Somatotopic Representation of Human Hand Muscles Using Magnetic Stimulation

S.S. HAGHIGHI and J.J. ORO (Columbia, U.S.A.)

We will describe mapping studies of human hand representation using magnetic stimulator in nine right-handed and one left-handed volunteers.

Magnetic stimulation (MS) was given with Cadwell MES-10 using a butterfly shaped (5 cm outside diameter) coil. MS were delivered at threshold intensities along vertex-tragus (VT) line on the right side. Recordings were from left abductor pollicis brevis (APB). A CRT monitor was used to track myogenic activation of individual digits and the forearm muscles during stimulation. Distances between stimulating locations were 1 cm apart. Amplitude and onset latency of the muscle responses were correlated with the location of the magnetic coil on scalp.

We obtained focal maps of the left APB without contamination from other adjacent muscles when magnetic coil was orientated on a line perpendicular to the VT line and intersecting C4 location. Maximal APB amplitude was recorded from multiple loci 2 to 3 cm anterior to C4 with an average 6 cm surface area. Prior facilitation of APB muscle did not change the location or the size of the map. The left-handed subject showed a larger map (8 cm surface area) for the APB muscle.

100.

A Randomized Trial of Diagnostic Test Sequencing in Multiple Sclerosis

P.W. O'CONNOR, A.S. DETSKY, W. KUCHARCZYK and C. TANSEY (Toronto, Ontario)

Background and Methods: We performed a randomized trial of the incremental impact of double-dose CT scan of the brain plus trimodal evoked potentials (EP-CT) versus magnetic resonance imaging (MRI) of the brain on neurologists' diagnostic labelling of patients with suspected MS. One hundred and sixty-three patients with suspected MS (clinically possible 44% or probable 46%-Poser criteria) were assessed by two neurologists. Patients were independently categorized by two neurologists into 1 of 4 groups (possible, probably, definite, or not MS) after reviewing the results of the diagnostic tests presented to them in 2 steps (MRI, EP-CT) in random order.

Results: Most change in diagnostic categorization occurred after presenting the first test result and was not significantly different between groups. However, significantly more patients were diagnosed as "not MS" or "definite MS" after step 2 compared to step 1, again irrespective of test sequence (P = .02). Within the EP-CT testing step the evoked potentials revealed abnormalities significantly more frequently than CT scan (P = .0001).

Conclusion: MRI scanning and EP-CT have comparable incremental effects on diagnostic decision-making in suspected MS when used alone. The combination of tests appears to influence labelling by clinicians significantly more than either testing protocol alone.

J. Neurobiology

101.

Detection of Rabies Virus Genomic RNA and mRNA in Mouse and Human Brains Using *In Situ* Hybridization

A.C. JACKSON, N. RINTOUL and W.H. WUNNER (Kingston, Ontario and Philadelphia, U.S.A.)

Rabies virus RNA was detected in mouse and human brains using *in situ* hybridization. ^{3}H-labeled single-stranded RNA probes were prepared, which were specific for genomic RNA and mRNAs coding for the 5 rabies virus proteins (N, NS, M, G, and L). Paraffin-embedded brains from human cases of rabies and mice experimentally infected with the challenge virus standard (CVS)-11 strain of rabies virus and street rabies virus were examined.

In CVS virus-infected mice, genomic RNA had a multifocal distribution in perikarya, perhaps reflecting concentration in viral factories. The mRNAs were more abundant than genomic RNA in CVS and street virus-infected mouse brains, and had a diffuse distribution in the perikarya. Similar amounts of signal were present for mRNAs coding for different rabies virus proteins.

In brains of human cases of rabies, genomic RNA was much more abundant than the mRNAs in infected neurons. This finding suggests either a relative block at the level of transcription or greater loss of mRNAs than genomic RNA during the agonal period, postmortem interval, or prior to penetration of fixative during immersion fixation. Studies on rabies virus-infected mouse brains showed that there was progressive loss of signals for genomic RNA and mRNA, which was more marked for mRNA, after postmortem autolytic periods of 12-72 hours. Signals may be greater for genomic RNA after postmortem autolysis because of the association of genomic RNA with proteins in the ribonucleoprotein complex.

102.

Immunosuppression with Monoclonal Antibodies in CNS Transplantation

C.R. HONEY and H.M. CHARLTON (Vancouver, British Columbia and Oxford, England)

The survival and function of neural xenografts were prolonged in two animal models immunosuppressed with monoclonal antibodies (mAb).

The hypogonadal (*hpg*) mouse is deficient in hypothalamic gonadotrophin releasing hormone (GnRH) with a consequent failure in post-natal gonadal development. Three groups of *hpg* mice had day 1 rat preoptic area neural xenografts (a source of GnRH neurons) transplanted to their third ventricle. Group 1 (N = 10) was immunosuppressed with an anti-CD4 MAb, Group 2 (N = 10)

received an anti-CD8 MAb and Group 3 (N = 10) received saline. Thirty days post-transplant, all animals in Group 1 had histologic evidence of surviving xenografts and half showed enlarged gonads. None of the animals in Group 2 or 3 had any evidence of surviving xenograft.

The hemi-Parkinson rat has been unilaterally lesioned to destroy the nigrostriatal dopamine system on one side. When stimulated with amphetamine, these animals rotate towards the lesioned side. This rotational behaviour can be abolished by transplanting dopaminergic neurons directly to the striatum on the lesioned side. Three groups of Wistar rats were lesioned. Groups 1 (N = 10) and 3 (N = 8) had human fetal mesencephalon neural xenografts[1] (a source of dopaminergic cells) transplanted to their striatum. Group 2 (N = 5) received hindbrain xenografts.[1] Groups 1 and 2 were immunosuppressed with an anti-interleukin-2-receptor (1L2R) MAb for 10 days while Group 3 received saline. Group 1 showed a significant reduction in rotation by one month post-transplant which continued for the duration of the experiment (six months). Histologic examination at this time showed surviving xenograft with abundant dopamine neurons. Groups 2 and 3 showed no reduction in rotation.

[1]approved by the Ethics Committee of the John Radcliffe Hospital, Oxford, U.K., and the British Medical Association.

103.

The Expression of Heat-Shock Protein (hsp72) in Cultured Human Brain Cells

M.S. FREEDMAN, N. BUU, D.C.G. RUIJS and J.P. ANTEL (Montreal, Quebec)

Interaction between the CNS and the immune system may involve recognition molecules other than those of traditional major histocompatibility complex (MHC) class I or II antigens, since the latter are not usually expressed within the CNS. Heat shock proteins (hsp), notably those of the hsp70 family, play a role in the chaperoning of plasma membrane associated molecules, (e.g. class II MHC plus processed antigen), to the surface of cells. Reactivity to hsp by lymphocytes has been noted, especially cells expressing the T cell receptor γ-δ gene rearrangement. Hsp72 has been found to be an inducible species in mammalian brain, with little expression in normal brain but a marked increase in expression following a heat stress to the animal. We therefore examined mixed human brain cell cultures to determine the differential hsp72 expression among the following cell types after a mild heat stress: astrocytes, microglia, oligodendroglia, and fibroblasts. We found that hsp72 expression was most easily induced in cultured oligodendrocytes, in keeping with the *in situ* data in mammalian brain which demonstrated induced hsp72 expression confined mostly to the white matter. This raises the possibility that oligodendrocytes might be more susceptible to damage induced by lymphocytes recognizing hsp, which has particular relevance to autoimmune diseases such as multiple sclerosis.

104.

Antagonism of CGRP and Substance P Receptors Lowers Blood Flow in the Endoneurium of Rat Sciatic Nerve

D.W. ZOCHODNE and LAM T. HO (Kingston, Ontario)

Vasa nervorum are innervated by adrenergic vasoconstrictive fibres and peptidergic fibres of unknown function. In other tissue beds vasoactive peptides from sensory fibres mediate neurogenic inflammation, but may also have a role in physiological vasoregulation. In previous work, we demonstrated that epineurial application of capsaicin induced prompt, sustained and intense endoneurial hyperemia from acute release of vasoactive peptides. Hyperemia was blocked and reversed by antagonism of SP (Substance P) or CGRP (Calcitonin gene-related peptide) receptors.

As in previous investigations, we serially studied blood flow (EBF) in the sciatic nerve of the rat using an endoneurial microelectrode sensitive to hydrogen clearance. After two normal EBF measurements we applied hCGRP (8-37) (Bachem, Torrance, CA), an antagonist of CGRP receptors and completed a further blood flow measurement with the antagonist in situ. After epineurial application of hCGRP (8-37), EBF fell below the previous control measurement and endoneurial microvascular resistance (EMR) increased (n = 6). In an identical protocol, spantide (SP antagonist (Sigma, St. Louis, MO)) also increased EMR and lowered EBF (n = 6). Both antagonists lowered EBF below control values published by ourselves and other workers using hydrogen clearance or other techniques.

We cannot exclude a direct vasoconstrictive action of hCGRP (8-37) or spantide on vasa nervorum. A more plausible mechanism may be that interruption of physiological CGRP and SP vasodilatation results in unopposed vasoconstriction and endoneurial oligemia. Our findings suggest that CGRP and SP have a role in normal tonic vasodilatation of epineurial arterioles supplying EBF.

105.

Dose Response Study of the Acute Effects of Nimodipine (Without Adjunctive Volume Expansion) on Spinal Cord Blood Flow and Electrophysiological Function After Spinal Cord Injury

I.B. ROSS and C.H. TATOR (Toronto, Ontario)

Nimodipine is an effective vasodilator with preferential action on the CNS. Recent experiments have demonstrated it to be effective at reversing post-traumatic ischemia and promoting electrophysiologic recovery in a rat spinal cord injury (SCI) model. These beneficial effects were achieved when nimodipine was combined with an agent to reverse post-traumatic hypotension, either a volume expander or a vasopressor. To determine if nimodipine alone can increase spinal cord blood flow (SCBF) and improve function after SCI, a dose response protocol was employed. Outcome measures included SCBF, and motor and somatosensory evoked potentials (MEP and SSEP). SCBF, MEP and SSEP were recorded before and after a 52 g clip compression injury at the T1 segment, and then repeated after nimodipine treatment. Experimental groups (n = 5 per group) received 35 min infusions of the following doses of nimodipine: 0; 0.005; 0.01; 0.025; and 0.05 mg/kg. SCBF decreased after injury in all groups. No increase in SCBF was seen after nimodipine infusion in any group. MEP and SSEP were abolished by the injury in all rats and no recovery was seen in any group.

Therefore, adjuvant vasopressor or volume expander therapy may be necessary for nimodipine to improve SCBF and promote recovery of function after SCI.

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106.

Electrical Field Mapping in the Normal Rat Spinal Cord

R.J. HURLBERT, C.H. TATOR and E. THERIAULT (Scarborough; Toronto, Ontario)

Direct current (DC) fields have been shown to possess beneficial effects in the treatment of acute spinal cord injury in animal models. However, little is known about the distribution of these fields within the spinal cord. We report results of field mapping in 5 normal rats.

Epidural disc electrodes were placed 10 mm apart under the lamina of C6 and T2. Stimulation consisted of a balanced 20 Hz sine wave, current limited by an on-line ammeter. Field strengths were measured with a lock-in differential amplifier and glass microelectrodes inserted directly into the spinal cord. Recordings were made from various positions and depths between the stimulating electrodes.

The relationship between stimulating current and field strength was linear; for a doubling of current there was a proportional doubling of measured voltage. The field strength was highest in close proximity to the stimulating electrodes; 14 μA of current produced voltages exceeding 1 mV/mm. At midpoint between the electrodes the measured field dropped to < 400 μV/mm in the spinal cord and < 200 μV/mm in the paraspinal musculature.

These results characterize the field distribution resulting from this type of stimulation in the normal spinal cord, and will help to determine the optimal stimulation parameters necessary to promote recovery following spinal cord injury in the rat.

K. Neuro-ophthalmology

107.

Singleton Leber's Hereditary Optic Neuropathy with White Matter Lesions and Oligoclonal Bands

W.A. FLETCHER and L. BARCLAY (Calgary, Alberta)

In August, 1989, a 34-year-old man noted blurring of vision when he jogged. By December, the blurring had become constant in his left eye. Examination showed a visual acuity of 20/20 OD and 20/400 OS, a left relative afferent pupil defect, bilateral small centrocoecal scotomata OD > OS, hyperemia of the left optic disc with telangiectatic and angulated vessels, and equivocal temporal pallor of the right disc. The findings suggested Leber's hereditary optic neuropathy (LHON) but none of 41 matroclinal relatives (19 males) had visual loss. By June, 1990 the patient's vision had deteriorated to < 20/200 OU. T2-weighted MR scans showed high-signal lesions in periventricular cerebral white matter and medulla. CSF showed oligoclonal bands. Testing for the LHON mutant of mitochondrial DNA (mtDNA) using SFaNI showed 98% mutant mtDNA in the patient, 90% in the mother, 40% in a sister and none in an uncle.

In many cases of LHON a point mutation in mtDNA at position 11778 causes substitution of histidine for arginine in NADH dehydrogenase. Mutant mtDNA can be identified by the cleavage patterns produced by endonuclease SfaNI or MaeIII. Previous studies of maternal relatives of singleton cases of LHON have suggested that pedigrees tend to become homoplasmic for mutant mtDNA. The differences in the proportion of mutant mtDNA between our patient's mother (90%), uncle (0%) and sister (40%) suggest that meiotic segregation toward normal mtDNA may explain the variable penetrance observed in some pedigrees.

The MRI and CSF findings in the present case suggest that multifocal CNS demyelination may occur in LHON. An MRI study reported no brain lesions in 13 patients with LHON but MR spectroscopy and brainstem evoked responses have shown evidence of subclinical brain dysfunction. The incidence of neurological abnormalities in LHON varies widely between pedigrees. These differences may relate to distinct mtDNA mutations.

108.

Relative Afferent Pupillary Defects from Midbrain Damage

J.A. SHARPE, M.J. MORROW and P.J. RANALLI (Toronto, Ontario; Los Angeles, U.S.A.)

Midbrain tegmental damage was confirmed by CT or magnetic resonance imaging in 9 patients who had relevant afferent pupillary defects. Five patients had infarcts, one a tentorial menigioma, one a cavernous angioma, and two had closed head injury. Six patients had vertical gaze palsies. This monocular light-near dissociation was detected by a swinging light test and quantified by neutral density filters. Monocular field and binocular hemifield stimulation revealed normal visual evoked potentials. Static perimetry showed normal fields in each eye of each patient. There was no optic atrophy or visible loss of retinal nerve fibres.

Relative afferent pupillary defects usually occurred contralateral the side of maximal midbrain involvement. However, in two patients the defect was on the side of the midbrain damage; in these patients the consensual reflex from the contralateral eye was also reduced, but there was no third nerve palsy. Involvement of the medial radix of the optic tract adjacent to the brachium of the superior colliculus, or the pretectal olivary nuclear region can explain the contralateral afferent defects with normal visual sensory function. Ipsilateral afferent defects in two patients are attributed to: 1) a greater proportion of decussating fibres from the contralateral pretectal nuclei to the ipsilateral Edinger-Westphal nucleus (EWN) than non-decussating fibres; and 2) a more ventral location of lesions, closer to the EWN, causing a prenuclear afferent defect with the consensual property of an "efferent" pupil defect.

109.

Retinotopic and Directional Smooth Ocular Pursuit Defects after Posterior Cerebral Hemispheric Lesions

J.A. SHARPE and M.J. MORROW (Toronto, Ontario; Los Angeles, U.S.A.)

Initial smooth pursuit responses to horizontal step-ramp targets were studied in 16 patients with unilateral lesions of the posterior cerebral hemisphere, using a magnetic search coil technique. Eleven patients had retinotopic defects consisting of low smooth pursuit velocities in both horizontal directions in the contralateral hemifield of vision. Two of these patients had intact visual fields. Four patients had directional pursuit asymmetry, consisting of reduction of smooth eye movement velocity ipsilateral to the lesion site when tracking a ramp target in both hemifields; only one of these four patients had asymmetry of pursuit maintenance during sinusoidal target tracking. In contrast, four patients had directional impairment of pursuit maintenance in response to sinusoidal targets, but no defects were identified with step-ramp targets. These two classes of pursuit defects, directional asymmetry and retinotopic defects, are similar to defects caused by lesions in areas MT (middle temporal)

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and MST (middle superior temporal) of monkey cerebral cortex. Four patients with retinotopic or directional pursuit impairment, but normal visual fields, had lesions involving Brodmann areas 19, 39, and 37, providing further evidence (Neurology 1990; 40: 284-292) that the posterior part of the angular gyrus and adjacent prestriate cortex comprise the human homologues of simian cortical areas MT and MST.

110.

Clinical Evidence Supporting an Immunological Basis for the Opsoclonus-Myoclonus Syndrome

A.A. WILFONG (Houston, U.S.A.)

Two individuals are presented who developed the opsoclonus-myoclonus syndrome. One also had myasthenia gravis and the other an occult hepatoblastoma. The occurrence of either condition with the opsoclonus-myoclonus syndrome has never been reported in the literature. Each of these rare associations offer insight into the pathophysiology of this fascinating disorder.

Immune-mediated myasthenia gravis occurred in a 13-year-old girl who had sequelae of an opsoclonus-myoclonus syndrome. She had an abnormal Raji Cell assay along with elevated anti-acetylcholine receptor and antithyroglobulin antibodies. No evidence of an associated malignancy was found with either condition. The co-existence of these two diseases strongly supports the hypothesis that the opsoclonus-myoclonus syndrome is immunologically mediated and that it can be added to the list of immune disorders that have been associated with myasthenia gravis.

Opsoclonus-myoclonus syndrome developed in an infant with Beckwith-Wiedemann syndrome. Screening studies for an occult neural crest tumor were negative. Computed tomographic scanning revealed a focal mass in the liver. Subsequent histological examination demonstrated an epithelial hepatoblastoma, with primarily embryonal differentiation. Current evidence suggests that a similar antigen epitope is expressed in the central nervous system (CNS) and in some primitive neoplasia, such as neuroblastomas and hepatoblastomas. In susceptible individuals, antibody cross-reactivity may lead to the development of an autoimmune response resulting in CNS injury and the opsoclonus-myoclonus syndrome.

111.

Esotropia and Epileptic Eye Deviation with Nystagmus

H.G. DUNN, A.M. TISCHLER and S.A. SMITH (Vancouver, British Columbia)

A girl of 9 years was found to have mild myopia. A month later she began to have "dizzy spells" lasting up to one minute with diplopia, in-turning of the right eye and jerk nystagmus on lateral gaze, more marked to the left, 10-15 times per day. CT scan of head proved normal. Three months later, uncorrected visual acuity in each eye had diminished to 6/60, and this could be corrected to 6/6 with myopic prescription. Intermittent right esotropia gradually increased to 40 prism diopters.

On examination 8 months after onset the patient described her "spells" as associated with a feeling that the eyes seemed to push towards the middle and with a sinking feeling, even when she was lying in bed. She was left-eyed by right-handed and right-footed. Optic fundi and pupils were normal. She was unable to abduct the eyes completely, with greater restriction on the right, while other eye movements were full. She had diplopia on lateral gaze and on looking upwards. No other neurological abnormalities were found. MRI scan of brain with use of gadolinium, was normal.

The first EEG three months after onset of symptoms showed only minor asymmetries. The second EEG 10 months after onset showed spike discharges in the left parietal-occipital region. During a third EEG a month later these discharges were noted again during wakefulness and had a dipole configuration. Two "dizzy spells" were recorded on videotape; there was generalized EEG suppression for about 12 seconds, followed by slowing in the left posterior quadrant involving the whole left hemisphere for about 15 seconds.

The girl's spinal fluid was normal, including amino acids, lactate and gammaglobulin, and no oligoclonal bands were demonstrable. Visual evoked potentials showed slight hyperactivity at the left occipital area. Brainstem auditory evoked potentials were mildly abnormal with lower amplitude on left-sided stimulation.

On treatment with carbamazepine in a dosage rising to 200 mg b.i.d. the spells stopped completely. The right esotropia also subsided, leaving a well-controlled esophoria of 25 prism dioptres, so that corrective surgery was not considered necessary.

It may be suggested that the ipsiversive deviation of the right eye and the nystagmus in this girl's seizures were due to epileptic activation of a smooth pursuit pathway. The almost complete preservation of consciousness in these spells was noteworthy. Some similar cases have been described as cyclic esotropia in the ophthalmological literature.

Poster Presentations
THURSDAY, JUNE 20, 1990

A. Neurobiology

P1.

Relationship between membrane potential and responses to Quisqualate and NMDA in Hippocampal Pyramidal Neurons In Vitro

P. FAN and J.C. SZERB (Halifax, Nova Scotia)

Insufficient energy supply is known to induce synaptic failure and neuronal death. It is now well established that two types of glutamate receptors are involved in these two processes: quisqualate (QUIS) in synaptic transmission, NMDA in neuronal death. Since ischemia, as well as hypoglycemia, produces first hyper-then depolarization, we investigated in transverse hippocampal slices the relationship between the current required to maintain a constant membrane potential in single-electrode voltage clamped CA1 pyramidal neurons and responses to QUIS and NMDA in a low (0.2-0.5 mM) glucose medium. QUIS and NMDA were applied in the perfusion fluid. Responses to QUIS and NMDA varied in opposite directions: during initial hyperpolarization, current induced by QUIS increased, while the effect of NMDA decreased. During subsequent depolarization QUIS induced inward current diminished or disappeared, while that induced by NMDA was potentiated. There was a linear relationship between responses to QUIS and the current required to maintain a constant membrane potential in the soma. Depolarization due to superfusion with 2-4 mM NH_4Cl, thought to be responsible for hepatic coma, also produced a depression of QUIS and an increase in NMDA response, which in contrast to the depolarization caused by low glucose, was fully reversible. The potentiation of NMDA response disappeared in Mg^{2+}-free media. It

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is concluded that depolarization of the subsynaptic membrane located in distant dendrites, which the somatic voltage clamp failed to control, is responsible for both synaptic failure and neuronal death. Not only do large amounts of glutamate appear in extracellular spaces during ischemia or hypoglycemia, but the resulting depolarization inhibits transmission and potentiates the neurotoxic effect of glutamate by removing the Mg^{2+} block of NMDA receptors.

Supported by: the MRC. P. Fan is an MRC Postdoctoral Fellow and Killam Scholar.

P2.

Epilepsy Model Using Domoic Acid

M.B. SUNDARAM, K. DAKSHINAMOORTI and S.K. SHARMA (Winnipeg, Manitoba)

We investigated the acute effects of domoic acid (DA) in adult Sprague Dawley rats.

Expt. 1: DA was injected in increasing doses into CA 3 region of right hippocampus in 5 rats. Brief ipsilateral spikes occurred within 1 minute after 1.80 ng and 3.80 ng injections. Spikes were bilateral after 7.50 ng. Clinical seizures occurred after 30 ng injection and were characterized by contralateral facial twitching, salivation, tachycardia and tachypnea. Clonic movements became bilateral and animals went into status epilepticus after 60 ng injection. Ipsilateral hippocampal GABA injection (10 nmol) suppressed spiking by Phenytoin was ineffective.

Expt. 2: In other rats, 30 ng DA injections decreased hippocampal GABA from 2.5 Mmol/g to 1.7 Mmol/g (mean; GABA measurements done at 150 minutes after DA).

Expt. 3: DA pulse (30 ng) in in vitro hippocampal slice experiments released 50% more glutamate than 50 mM Kcl pulse.

Conclusions: i) DA in rats produces consistent, dose related EEG changes and seizures; ii) DA appears at least 20 times more potent than kainic acid; iii) DA decreases hippocampal GABA but augments glutamate release.

P3.

Evidence for Increased Mesocortical Dopaminergic Function in Portal-Systemic Encephalopathy

R.F. BUTTERWORTH, M. BERGERON, M.S. SWAIN and T.A. READER (Montreal, Quebec)

Portal-systemic encephalopathy (PSE) is associated with a variety of neuropsychiatric symptoms such as confusion, changes in personality as well as sleep and memory disturbances. Hyperammonemia and changes in brain monoamine metabolism have been proposed to contribute to alterations in consciousness and neurological status in human hepatic encephalopathy (Bergeron et al., *Neurochem,. Res.*, 14, 853, 1989). Portacaval anastomosis (PCA) in the rat results in sustained hyperammonemia and increased plasma and brain levels of phenylalanine and tyrosine. Administration of ammonia to rats with PCA precipitates severe signs of HE progressing through loss of righting reflex to loss of consciousness and ultimately deep coma. To evaluate the relationship between the degree of neurological impairment and dopamine (DA) metabolism, the levels of DA and its metabolites were measured by HPLC with electrochemical detection in different brain regions in rats with PCA at various stages of HE after administration of ammonia, and in sham-operated controls. Results show increased DA metabolites/DA ratios after PCA and ammonia loading, in anterior cingulate and piriform-entorhinal cortices as well as in the raphe nuclei. These ratios were found to be unchanged in the caudate-putamen. These results suggest a region-selective increase of DA turnover indicating a possible hyperactivity of the mesocortical dopaminergic fibres. Dysfunction of the mesocortical dopaminergic system could be involved in the etiology of neuropsychiatric symptoms observed in human PSE.

Funded by: FRSQ and MRC Canada

P4.

Influence of Development and Aging on the Release of Superoxide Anion Radical and Hydrogen Peroxide from Isolated Rat Cerebral Mitochondria

R.F. DEL MAESTRO and W. McDONALD (London, Ontario)

The hypothesis that the succinate-supported extramitochondrial release of superoxide anion radical (O_2^-) and H_2O_2 by isolated murine brain mitochondria would be influenced by development and aging has been tested.

Mitochondria were isolated from Wistar rat forebrain structures of animals from 2 to 365 days of age. Hydrogen peroxide was assessed by enzyme-coupled spectrofluorometric method and an estimate of simultaneous O_2^- release was obtained by adding superoxide dismutase to convert O_2^- to H_2O_2.

The results demonstrate that aging in the Wistar rat is associated with increasing extramitochondrial O_2 and H_2O_2 release by isolated brain mitochondria.

Hydrogen peroxide and O_2^- release were non-detectable at 2 and 12 days of age increasing to 1.49 nM/min/mg protein H_2O_2 and 3.31 nM/min/mg protein of O_2^- at 365 days. The proportion of O_2^- release compared to H_2O_2 release increased with aging.

Development and aging in the Wistar rat brain is associated with increasing extramitochondrial release of O_2^- and H_2O_2 when succinate was used as a substrate. Development and aging was associated with greater increases in O_2^- extramitochondrial release than H_2O_2 extramitochondrial release.

P5.

A Simple Organotypic Whole-Mount Spinal Cord Culture System for Fluorescence-Ratio Imaging of Intracellular Calcium

M. TYMIANSKI, E. THERIAULT, C.H. TATOR and I. SPIGELMAN (Toronto, Ontario)

Spinal cord injury (SCI) causes a rise in intracellular calcium levels [Ca++]i. This phenomenon is difficult to study *in-vitro*. Dissociated neuronal culture models of CNS trauma lack many properties of an *in-vivo* system. However, assessment of [Ca++]i levels with fluorescence ratio imaging (FRI) requires cellular monolayers achieved only in tissue culture settings. We report a tissue culture technique designed to overcome some drawbacks of current models.

Whole spinal cords were dissected from embryonic mice and divided into cervical, thoracic and lumbar segments. Each segment

was mounted on a glass coverslip, placed in a culture tube containing culture medium, and set in a roller-drum rotating at ten rev./hour. Feedings took place bi-weekly. Within 21 days, the explants thinned out to a mono-layer. Explants survived in this state for over 7 weeks.

Culture yields were characterized by morphologic assessment, immunocytochemical staining (anti-somatostatin, neurofilament, neuron-specific enolase, GABA, GFAP, ChAT and substance P), and electrophysiologic (whole-cell patch-clamp) techniques.

Free [Ca++]i measurements were performed by FRI using the Ca++ indicator Fura-2. Resting [Ca++]i in large neurons were in the 80nM range and increased several fold upon depolarization with 50mM KCL or application of ionomycin.

We believe that this culture setting approximates more closely the neuronal micro-environment, while maintaining easy access for Ca++ imaging and electrophysiologic manipulation. This is helpful in the study of cellular events in SCI.

P6.

The Effects of Neuroleptics on the Neuronal Unit Activity of the Prefrontal Cortex in the Rat

R. GODBOUT, J. MANTZ, S. PIROT, A.-M. THIERRY and J. GLOWINSKI (Montreal, Quebec; Paris, France)

The prefrontal cortex (PFC) is involved in the regulation of emotional states, the control of motor activity and the management of cognitive processes. The PFC is innervated by dopaminergic (DA) neurons of the ventral tegmental area (VTA) and by serotoninergic (5-HT) neurons of the midbrain raphé nuclei (RN). We analysed the effect of selective DA and 5-HT receptor antagonists on the firing inhibition induced in PFC neurons following VTA and RN stimulation in anesthetized rats.

Electrical stimulation of the VTA at 1Hz inhibited PFC spontaneous firing in 78% of 225 cells tested, for an average of 110ms. This was reversibly blocked by microiontophoretic applications of DA D_2 receptor antagonists sulpiride (61% of the 48 cells tested), RIV 2093 (88% of 16 cells), and LUR 2366 (88% of 8 cells). VTA-induced inhibitions were still present upon the application of the selective D_1 antagonist SCH-23390 (n = 11). The control applications of the β–(propranolol; n = 11), α_1–(prazozin; n = 7) and α_2–(yohimbine; n = 13) adrenoreceptor antagonists were also without effects. The stimulation of the median RN (1Hz) inhibited 53% of 210 spontaneously active PFC neurons for an average of 82ms. This was blocked reversibly by acute i.p. administrations of the 5-HT_2 receptors antagonists ketanserin (9/11 neurons), ritanserin (4/5 neurons) and RP-62203 (8/10 cells) at doses of 1 to 4 mg/kg. Inhibitions induced by VTA stimulation in the same cells were not affected, showing the specificity of the observed blockades.

These results show that selective receptor antagonists can block the inhibitory effects of endogenously-released DA and 5-HT on the firing activity of PFC neurons. It has been proposed that disorders in DA and 5-HT are responsible for the clinical manifestations of thought disorders such as schizophrenia. The present observations obtained with neuroleptics support this contention.

Supported by: INSERM, FRSQ, and CAFIR (U. de Montréal)

B. Neurosurgery

P7.

HLA Antigens in Familial Cerebral Aneurysms

R. LeBLANC, ANDRÈS M. LOZANO and RONALD GUTTMANN (Montreal, Quebec)

It has been suggested that specific HLA antigens, most notably A28, B7 and DR2, may be associated with cerebral aneurysms, suggesting a genetic etiology for cerebral aneurysms, perhaps related to a gene encoded on chromosome 6.

To test the hypothesis that familial cerebral aneurysms are co-inherited with specific HLA-antigens or haplotypes we typed the LHA antigens of 2 families with familial cerebral aneurysms. Six individuals (3 in each family, all females) had 9 proven aneurysms and 8 of their siblings had negative 4-vessel angiograms.

There was no specific HLA antigen or inheritance of specific HLA haplotype that correlated with the presence of cerebral aneurysms. Although HLA-B7 and DR2 were present in patients with aneurysms they were also present in patients with negative angiograms, and absent in the 2 patients with multiple aneurysms. HLA-A28 was absent in all family members. Individuals with the same haplotype could or could not have cerebral aneurysms.

HLA typing is not sufficient to identify or exclude family members at risk of having a cerebral aneurysm.

P8.

Pre-operative Speech Mapping with Functional-Activation Positron Emission Tomography

R. LeBLANC, ERNEST MEYER, DANIEL BUB, ROBERT ZATORRE and ALAN EVANS (Montreal, Quebec)

The pre-operative localization of primary speech areas in patients harboring structural brain lesions has not previously been described. We report the first instance of the use of 3-dimensional Magnetic Resonance Imaging (MRI) anatomically correlated to Positron Emission Tomography (PET) scanning to identify these areas in a patient with an arteriovenous malformation (AVM) in the posterior speech region.

The patient was a 24-year-old right-handed female with an angiographically proven 3-4 cm. AVM localized by MRI to the left mid- and posterior 2nd and 3rd temporal convolutions, and in whom the intracarotid injection of Amytal produced significant language disruption. On the basis of – perhaps apocryphal – reports of intrahemispheric migration of language function from the classically described speech regions in patients with AVMs we tested the hypothesis of such a functional shift in this patient by activation-PET scanning. A baseline PET-cerebral blood blow (CBF) study identified the AVM and an activation-PET scan performed during reading and speaking of simple words showed increased activity in the primary visual centres bilaterally and in the visual associative area on the left, in the left mid-temporal region – Wernicke's area – as a crescent about the AVM.

These data confirm that activation-PET scanning can lateralize and localize the primary and associative speech regions, and falsify – in this case – the hypothesis of functional migration within a hemisphere harboring an AVM in a primary speech region.

We conclude that mapping of sensory-motor areas, as we have previously described (Journal of Neurosurgery, October, 1990), and of language areas as described here is reliable and useful in the pre-operative assessment of patients with cerebral AVMs.

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P9.

Excision of Arteriovenous Malformations in Sensorimotor and Language-Related Neocortex Using Stimulation Mapping and Corticography Under Local Anesthesia

J.P. GORECKI, ROBERT R. SMITH and ABELARDO S. WEE (Jackson, U.S.A.)

Arteriovenous malformations (AVMs) are dealt with using a variety of techniques including, direct excision (attacking arterial feeders or by retrograde isolation) controlled hypotension, endovascular intervention, stereotactic irradiation, staged operations and direct cortical mapping. Rolandic AVMs are particularly challenging. Compromise of vascular supply to normal surrounding brain or direct trauma to eloquent neocortex may result in unacceptable neurological morbidity. In patients with epilepsy, failure to excise areas of epileptogenic brain as identified by corticography may result in continued seizures, after successful obliteration of the AVM. In this report, we describe two patients who underwent excision of large Rolandic AVMs under local anesthesia. One lesion was located in the dominant (left) hemisphere. Both patients underwent pre and post operative neuropsychological evaluation. The WADA test was not performed since there was no language ambiguity. Electrocorticography was used to identify epileptogenic brain. Stimulation-mapping techniques were used to identify critical motor, sensory and language areas. The resection was carried out at the same procedure allowing ongoing testing of neurologic function as feeding vessels were taken. Both patients demonstrated delayed, transient deficits as anticipated which resolved over seven to fourteen days. Cortical mapping under local anesthesia is beneficial for resection of certain AVMs located in eloquent areas and it is not necessary to perform a second operation under general anesthesia to excise the lesions.

P10.

***Relief of Chronic Pelvic Pain Through Surgical Lesions of the* Conus Medullaris Dorsal Root Entry Zone**

J.P. GORECKI, TRAVIS BURT and ABELARDO S. WEE (Jackson, U.S.A.)

Dorsal root entry zone (DREZ) lesions are effective in treating specific pain syndromes, most notably post-brachial plexus avulsion. There is limited experience, however with lesions in the conus medullaris. We review the case of a patient having pelvic pain and urinary retention who failed to improve despite multiple prior interventions. Her pain was completely relieved after DREZ lesions were placed bilaterally at S2, S3, S4 and S5. The intraoperative sensory and motor evoked potential monitoring used to define the level is described in detail.

P11.

Post-Traumatic Ligamentous Disruption of Cervical Spine: An Easily Overlooked Diagnosis: Three Case Presentation

M. FAZL, J. LaFEBVRE, R.A. WILLINSKY and S. GERTZBEIN (Toronto, Ontario)

Three cases of hyperflexion sprain of the cervical spine secondary to motor vehicle accidents are discussed. One patient presented with quadriplegia while the other two only had upper and/or lower extremities paresthesia at the scene of the accident. All patients were young with no evidence of degenerative disc disease or osteoarthritis. Diagnosis of hyperflexion sprain is suggested by transient or persistent neurological deficits, local tenderness, or plain film findings which include interspinous fanning, localized kyphotic angulation, subluxation or disc space narrowing. Review of our cases revealed some of these findings on initial presentation. In cases where there are no neurological deficits, controlled flexion and extension views following routine plain films may be diagnostic or an unstable cervical spine. If there is a persistent neurological deficit, MRI is the examination of choice. If there is no compression of the thecal sac or spinal cord supervised flexion and extension views of cervical spine should be done. Definitive management of the unstable spine is operative fixation.

P12.

Cervical Myelopathy Due to Ossification of Posterior Longitudinal Ligament in a Caucasian

F.B. MAROUN, P. PERKINS, A. MAKINO, R. ARTS, M. MANGAN and J.C. JACOB (St. John's, Newfoundland)

Cervical myelopathy due to ossification of posterior longitudinal ligament (OPLL) is very rare in a Caucasian and has been seldom reported.

A 65-year-old lady of British descent suffered from cervical myelopathy caused by massive cervical OPLL. The patient had a history of slowly progressive gait disturbance, paresthesia in both legs and recent urinary urge incontinence. Radiological examination showed a continuous OPLL from C5 to C7 and complete block of contrast at this level. Since MRI scan has little diagnostic value, a three-dimensional CT image was obtained and provided clear visualization of the lesion. An anterior vertebrectomy of C5 to C7 and removal of OPLL with subsequent fusion of C4 to T1 by using a free fibula graft was successfully achieved. Her gait disturbance improved and paresthesia of legs and urinary symptoms disappeared after the surgery. Benefits of three dimensional display of the lesion is emphasized together with review of the literature.

P13.

Progressive Myelopathy from an Occult Non-United Odontoid Fracture

R.J. MOULTON and P.J. MULLER (Toronto, Ontario)

This report describes the clinical presentation and surgical management of a patient presenting with progressive myelopathy resulting from non-union of a previously unrecognized odontoid fracture.

The patient is a 78-year-old man who presented with mild quadriparesis in May 1990. X-rays of the cervical spine showed posterior subluxation of C1 on C2, and the odontoid process could not be clearly identified. There was no history of trauma. Over the summer months the patient's quadriparesis increased. The patient was admitted to hospital in Oct. 90, and at that time was wheelchair-bound and could feed himself only with difficulty. An MRI scan showed a large soft tissue mass in the area of the odontoid with marked anterior compression of the cervico-medullary junction. Plain x-ray films showed a remnant of odontoid, and some movement at C1-C2 with flexion and extension of the neck.

Surgical management consisted of reduction of C1 on C2 with gentle traction, and subsequent transoral resection of the remnant of odontoid and a mass of fibrous tissue surrounding it, followed by posterior fusion under the same anaesthetic.

At 11 weeks after operation the patient was discharged home. He was ambulating independently and cared for himself with minimal assistance.

P14.

BRW Stereotactic Biopsy: A Report on 90 Procedures

P.J. MULLER, J. BILBAO, WM. TUCKER and R. MOULTON (Toronto, Ontario)

We have carried out 90 BRW stereotactic procedures in 85 patients in the 3 years from 1988-1990. There were 55 males and 30 females; their mean age was 50 ± 16 years.

Precraniotomy stereolocalization was carried out in 7 cases [4 with brain tumour, and one each with brain abscess, intracerebral hemorrhage and cavernous angioma]. All seven procedures were successful in localizing the lesion for subsequent craniotomy.

In 83 procedures the purpose was biopsy only. Twelve patients who were HIV positive underwent a total of 14 biopsies. These patients usually came to biopsy after failure of response to antitoxoplasmosis treatment.

In the remaining 66 patients [69 biopsies], the presumptive diagnosis was brain tumour. In these 69 procedures a histological diagnosis was achieved in [87%]. There were 58 tumours, and one each of infarct and cavernous angioma. The distribution of the 58 tumours was 37 astrocytic, 5 glioma [cell type unspecified], 4 meningiomas, 4 lymphomas, 6 metastases, 1 neuroblastoma, and 1 tumour of unspecified origin. Of the astrocytic tumours a grading was given in 86% as follows: 6 grade-4, 13 grade-3 and 13 grade-2.

In 9 cases where the preoperative presumptive diagnosis was tumour no specific diagnosis was made. In 3 cases tissue was submitted that did not appear abnormal; one proved to be a lymphoma on second biopsy, one proved to be a metastases at craniotomy and one proved to be an infarction on CT and clinical follow-up. In one case no tissue was submitted because cyst drainage altered the tumour configuration; glioma was diagnosed at second biopsy. In 5 cases the diagnosis of gliosis or glial proliferation was made without evidence of neoplasia; they remain tumour suspects.

There were 10 patients who had a neurological decline postbiopsy. In 6 cases the complication was intracranial hemorrhage, fatal in one case, and in 4 the complication was cerebral swelling. Of these 10 patients, the neurological deficit attributable to the biopsy recovered in all but 4 with steroids, surgery or spontaneously. The procedure morbidity rate was 10% [9/90]; the permanent deficit rate was 4% [3/84] and the procedure mortality rate was 1% [1/90].

P15.

Spontaneous Spinal Epidural Hematoma Causing Paraplegia. Resolution and Recovery Without Surgical Decompression

D. CLARKE, GILLES BERTRAND and DONATELLA TAMPIERI (Montreal, Quebec)

Spontaneous spinal epidural hematoma is a well recognized but rare entity, the standard treatment of which has been the urgent surgical evacuation of the hematoma. The authors report a case of a 76-year-old man who precipitously became paraplegic secondary to a spontaneous spinal epidural hematoma, and who subsequently experienced complete resolution of his neurologic deficit and of the hematoma. They conclude that conservative (nonoperative) management of spontaneous spinal epidural hematoma may be appropriate in those instances where there is early and sustained neurologic recovery confirmed by radiologic resolution of the lesion.

P16.

Why Residents Leave Neurosurgical Training

M. CUSIMANO, W.S. TUCKER and A. YONKE (Toronto, Ontario; Chicago, U.S.A.)

Attrition of residents from surgical residency programs has not previously been studied. This study was designed to gain insight into resident's motivations for leaving neurosurgery.

Structured interviews were conducted with those residents who voluntarily withdrew from neurosurgical training ("leavers") since 1984. Questionnaires containing similar questions were sent to the last thirty trainees to complete training ("graduates") as well as those who were presently in training ("residents") at this particular training program.

Motivations and aspirations for training in neurosurgery were similar at the beginning of training for all groups. All groups report similar adverse stresses during training. However, those who leave training appear to be so influenced with adverse factors in the environment that their goals change toward a similar area of interest but one with a completely different social system (all but one leaver transferred from neurosurgery to a neuro-imaging specialty). Those who complete training report extremely strong goal commitments to complete a task to which they have committed themselves.

Resident attrition from neurosurgery seems more related to factors intrinsic to training and peculiar to the established social systems in a particular residency rather than factors considered as important selection criteria for residents. These findings suggest that until new, more sensitive and more specific methods for selecting residents are developed, program directors interested in lessening attrition from their programs should allocate energies towards factors that keep residents in training.

P17.

Lumbo-Peritoneal Shunts — Do They Really Work?

I.P. CHAMBI, MICHAEL CUSIMANO, BRUCE HENDRICK, HAROLD HOFFMAN and ROBIN HUMPHREYS (Orange, U.S.A.; Toronto, Ontario)

Lumbo-peritoneal shunting is a reasonable alternative when dealing with communicating hydrocephalus. In the literature, there is no reference to the rate of shunt patency related to the etiologic factor. This study was undertaken to identify a subgroup of patients with communicating hydrocephalus who would most benefit from lumbo-peritoneal shunting.

This review included 58 patients with symptomatic hydrocephalus with a medium follow-up of 8.4 years from ages one month to nine years, in whom a head CT scan demonstrated a communicating hydrocephalus. The associated pathological abnormalities causing communicating hydrocephalus are as follow: intraventricular hemorrhage 11, congenital 13, unknown 14, infection 5, trauma 13 and post-operative 2.

Surgical Approach: 37 patients underwent a "T" tube shunting through a limited laminectomy, complications were infection in 2 patients, acquired Chiari I and one overshunting in 2 patients. The complications seen using the Touey needle and straight tubing tech-

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nique, were infection in one patient, CSF leak in one and overshunting in two. The latter approach has proven to be easier to perform and it is associated with fewer complication, however both techniques are effective and safe.

The patency rate, when the cause for communicating hydrocephalus was unknown was 6 years, congenital 5.6 years, trauma 5 years, infection 2.4 years, post-operative 2 years and when the cause was intraventricular hemorrhage, the patency rate was only 0.9 years. At surgery shunt malfunction due to blockage was seen in 22, migration in 5 and a broken shunt in 3 patients.

This study indicates that a consistent, long term patency rate can be achieved when the etiology for communicating hydrocephalus is unknown. On the other hand, a poor shunt patency rate is seen in patients with intraventricular hemorrhage.

P18.

Complications Associated with Aggressive Management of Head Injuries

D.S. MALLOY (Halifax, Nova Scotia)

Aggressive ICU management of head injury appears to be associated with improved outcome. Aggressive management in our unit includes ICP monitoring, ventilatory support and invasive hemodynamic monitoring. A review of our experience with complications of this approach is presented.

P19.

NMR Spectroscopic Analysis of CSF in Traumatic Brain Injury

D. LOUW, D. MALLOY, G. SUTHERLAND and J. PEELING (Halifax, Nova Scotia; Winnipeg, Manitoba)

Traumatic brain injury (TBI) may result in profound perturbation of cerebral anatomy and neurochemistry. This is invariably reflected in alterations to CSF chemistry. Previous human studies, however, have tended to be narrow, often only measuring a single component; eg. CPK. The technique of proton NMR spectroscopy, in contradistinction, allows for simultaneous measurement of multiple metabolites.

CSF samples have been collected daily from the ventricular drains of eight patients with severe head injury. The CSF was subjected to spectroscopy, and the sequential spectra thus generated were analyzed in relation to appropriate clinical parameters such as ICP, GCS and GOS. We will present our data correlating CSF chemistry with clinical outcome.

P20.

Stereotactic Craniotomy Using the Leksell System: Illustration with 2 Cases

J.-G. VILLEMURE and J. ESPINOSA (Montreal, Quebec)

Stereotactic craniotomy provides precision in the approach to certain intra-cerebral lesions. The authors describe two cases where the procedure was used successfully for the removal of cysticercosis lesion in the posterior right frontal lobe and the removal of cavernous angioma located in the left caudate nucleus.

The methodology consists first in obtaining in stereotactic condition a localization with computerized CT scan following which a craniotomy is carried out under stereotactic condition and the approach guided by the coordinates obtained and the location of the lesion. Small cortical incision and direct approach as far as the direction can be carried out with this guidance system. Brain resection is minimal as well as retraction.

While many cases have been reported of stereotactic craniotomy using the DRW equipment, and this mainly by Dr. P. Kelly, there have been a few cases of stereotactic craniotomy reported using the Leksell system.

For deep-seated lesions or for lesions located to very eloquent area, precision in localization to minimize the disturbance of surrounding brain is necessary and stereotactic craniotomy offers these advantages. It certainly may be an alternative to real time ultrasonography.

P21.

Transient Abducens Palsy Following Shunting for Hydrocephalus

J. ESPINOSA, M. CIROUX, K. JOHNSTON, T. KIRKHAM and J.G. VILLEMURE (Montreal, Quebec; Toronto, Ontario)

Over the years a significant number of complications have been associated with shunting procedures. However, to our knowledge, transient 6th cranial nerve palsy has been described only on few occasions.

From July 1978 to December 1990, 80 patients underwent shunting procedure (V.A. and V.P.) for N.P.H. All procedures were performed by the senior author (J.G.V.). Three patients developed diplopia on horizontal gaze after surgery. All patients were male, age ranges from 67 to 69 years and the onset of symptoms was 7-14 days after surgery.

One patient had a right 6th nerve palsy and the other two developed bilateral 6th nerve palsy. The symptoms disappeared completely 11 weeks after surgery in the patient with unilateral involvement; the other two patients have improved significantly 8 and 9 weeks after the surgical procedure.

We believe that transient abducens palsy in these patients was caused by reduction in the amount of C.S.F. at the basal cisterns and sub-arachnoid space after the ventricular derivation allowing caudal displacement of the brain creating direct traction on the abducens nerve. Pre and post-operative magnetic resonance will illustrate the mechanism.

P22.

Abces Cerebral A Nocardia. A Propos de Trois Cas.

D.L. LADOUCEUR and RAYMOND DUPERVAL (Sherbrooke, Quebec)

La nocardiose cérébrale peut se présenter par des abcès uniques ou multiples, le plus souvent suite à une infection pulmonaire à Nocardia Astéroides.

Trois patients porteurs d'un abcès cérébral unique à Nocardia sont présentés. Deux de ceux-ci se sont manifestés par une atteinte pulmonaire initiale, dont un souffrait de protéinose alvéolaire. Le troisième cas a d'emblée présenté des symptômes d'atteinte cérébrale sans manifestation pulmonaire, et n'était pas immunosupprimé.

Le traitement chirurgical complété par une antibiothérapie endoveineuse a eu raison de l'agent envahisseur.

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P23.

Spontaneous Disappearance of an Intracranial Aneurysm after Subarachnoid Hemorrhage

M. HAMILTON and O.N.R. DOLD (Calgary, Alberta)

Cases of incomplete and complete disappearance of intracranial aneurysms have been reported although the incidence of this event following subarachnoid hemorrhage (SAH) is extremely uncommon. We present angiographic evidence of spontaneous disappearance of an aneurysm following SAH and discuss the management strategies available to a neurosurgeon.

A 29-year-old female presented with a SAH (Grade V) in January, 1988. Angiography identified a 5mm anterior communicating artery aneurysm. Her clinical course was complicated by severe delayed ischemic deficit (vasospasm) with cerebral infarction. No antifibrinolytic agents were used. This left the patient quadriparetic, dysphasic and cognitively impaired. Operative intervention was declined by the family.

During the 14 months she underwent remarkable improvement. She now has a near normal cognitive evaluation and walks with assistance. The patient requested surgical treatment. Follow-up angiography demonstrated that all cerebral arteries were patent. No aneurysm was identified despite multiple injections and views. Spontaneous thrombosis of the aneurysm was diagnosed.

The spontaneous disappearance of this aneurysm is not unique but the majority of such described cases usually involves either a giant aneurysm or patients treated with antifibrinolytic agents after SAH. Of great concern to the neurosurgeon are the reports of aneurysms which have disappeared only to reappear. These particular cases typically occur in close proximity to the original SAH. It is essential that the neurosurgeon be aware of this possibility. In this case it is postulated that the spontaneous thrombosis occurred during the course of her vasospasm. However no further investigation is planned given the extended time period since her SAH. The probable mechanisms of spontaneous disappearance of intracranial aneurysms will be reviewed.

P24.

Cerebral Venous Pressure Monitoring in Patients with Arteriovenous Malformations

M.C. WALLACE, R. WILLINSKY and K. TERBRUGGE (Toronto, Ontario)

Patients with arteriovenous malformations of the brain have arteriovenous shunting which results in an elevation in cerebral venous pressure. Often, this elevation in pressure (cerebral venous hypertension) impedes cerebral venous return and may be the explanation for neurological deficits in such patients. Advancing endovascular catheter techniques permit selective catheterization of cerebral arteries and veins and our group has started to use physiological pressure monitoring, arterial and venous, in patients with brain arteriovenous malformations. A case illustrative of the potential use of this monitoring is described.

A 50-year-old man underwent translabyrinthine resection of an acoustic neuroma. Years later, he presented with global neurological dysfunction secondary to a dural arteriovenous malformation of the occluded ipsilateral sigmoid sinus. A stenosis of the contralateral transverse sinus was also detected. During endovascular embolization procedures, arterial and transverse sinus pressure recordings were made simultaneously. Middle meningeal and occipital arteries feeding the malformation demonstrated a pressure of 75/50 mmHg in the face of a systemic arterial pressure of 130/80 mmHg. Venous pressure was markedly elevated in the ipsilateral transverse sinus (45/38 mmHg). However, the stenosis in the contralateral transverse sinus contributed to the cerebral venous hypertension, demonstrating a physiological gradient of 30mmHg. Sequential embolization of arterial cerebral venous pressure, permitting safe sacrifice of the transverse sinus with coil installation.

The case demonstrates the feasibility of cerebral venous recording and the potential use of pressure gradient recording to assist with therapeutic decisions.

P25.

University of Toronto Brain Vascular Malformation Study Group: Advantages of a Multidisciplinary Approach

M.C. WALLACE, F. GENTILI, M. SCHWARTZ, K. TERBRUGGE, R. WILLINSKY and C. YOUNG (Toronto, Ontario)

The multidisciplinary treatment program for patients with brain vascular malformations was established at the University of Toronto in 1989. The group consists of neurosurgeons, neuroradiologists and radiation oncologists. Close working relationships have been established with both neuropsychology and social work.

A weekly clinic reviews between 6-10 patients (and now has catalogued more than 200 patients) with brain vascular malformations. History and physical exams are recorded and the investigations to date are reviewed at each visit. Further investigations such as magnetic resonance imaging or outpatient angiography are scheduled. The particular cases are conferenced monthly by the entire study group, and discussed with the patients at a later clinic appointment. The therapeutic options discussed include observation, interventional radiology, neurosurgery, stereostactic radiosurgery or a combination of therapies. Education regarding the alternatives is provided to the patient and referring physician.

Advantages to such a program have revolved around physician communication and patient education. Questions regarding investigations or therapy can be addressed by different disciplines at a single clinic visit. The valuable role and need for expertise in neuropsychology, social work and seizure control have become apparent. Many referrals for consideration of a specific therapy have been conferenced, with subsequent recommendation of an alternate therapy. For example, there have been more than 50 referrals for consideration of radiosurgery, over 50% of which have undergone either endovascular or neurosurgical procedures as an individual treatment or as a staged treatment prior to radiosurgery.

The clinic provides an ideal forum for data collection for such an uncommon disease process. It is the goal of the group to improve clinical care and answer epidemiological and therapeutic questions about patients with brain vascular malformations.

P26.

Methodologic Guidelines for Randomized Clinical Trials of Surgical Procedures

J.R.W. KESTLE, M.N. LEVINE and D.L. SACKETT (Toronto; Hamilton, Ontario)

The assessment of the efficacy of an operation poses some unique difficulties which are not encountered in medical trials. These difficulties are outlined and their importance is assessed in a sample of published surgical trials.

The methodologic problems that are unique to surgical trials are:

1) The skill of the surgeon influences the manoeuvre,

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2) The technique for the manoeuvre differs for each surgeon,
3) The manoeuvre includes more than the operation,
4) The intended goal of surgery is not always achieved,
5) Blinding is usually impossible,
6) Accrual may be difficult.

We have reviewed 35 randomized trials of surgical procedures to assess the effect of these difficulties. Based on this review, the following recommendations are made:

1) Describe the surgeons' experience with the procedure being tested,
2) Describe the technique in sufficient detail to allow its replication,
3) Describe the peri-operative care in sufficient detail to allow its replication,
4) Include a post-operative assessment of "surgical compliance",
5) Assess outcome with "hard" measures or independent assessors,
6) Describe the eligible non-randomized patients.

Greater attention to these issues during the conduct and reporting of surgical trials is recommended.

C. Neuro-oncology

P27.

De Novo Gliosarcoma Six Months After Resection of an Arteriovenous Malformation

R. LeBLANC, G.B. GOPLEN and Y. ROBITAILLE (Montreal, Quebec; Saskatoon, Saskatchewan)

We report the *de novo* development of a gliosarcoma in the resection bed of an arteriovenous malformation (AVM) six months after resection, indicating the time-frame within which the latter can develop within the brain.

A 69-year-old woman was initially assessed at age 53 following the new onset of seizures. Investigations demonstrated a right postero-inferior parietal AVM with no other anomaly. Her seizures were well controlled with anticonvulsants. She was seen again in 1990, at age 69, following a cerebral hemorrhage from rupture of the AVM documented by computed tomography (CT) scanning. Reinvestigation again demonstrated the AVM but no other associated anomaly was seen even on magnetic resonance imaging (MRI). The AVM was resected en bloc. The associated brain tissue demonstrated only neuronal loss and gliosis. She was well until six months later when she developed status epilepticus. A non-infused CT scan demonstrated right hemisphere white matter edema and her anticonvulsants were increased. Two weeks later she acutely developed a left hemiplegia. CT scanning demonstrated marked cerebral edema and a multiloculated ring-enhancing lesion with mural nodules centred around the resection bed of the AVM as demonstrated by the identification of vascular clips placed at the initial surgery. At craniotomy a necrotic glioma within the AVM resection bed was encountered which on histological examination had all the classic features of gliosarcoma.

The association of AVMs and cavernous angiomas with glial tumour is rare. Rarer still is the development of a glial tumour at the site of a previous AVM. The biological basis of this association is discussed. Our case provides insight into the biology of gliomas, indicating that a *de novo* gliosarcoma can develop and become floridly symptomatic within 6 months.

P28.

Intracranial Malignant Epithelioid Trigeminal Schwannoma

D.M.S. IZUKAWA, B.K. TEMPLE and J. MANOWSKI (Mississauga, Ontario)

Trigeminal schwanommas comprise 0.1-0.4% of intracranial tumours. They may arise from the trigeminal root, ganglion or peripheral branches, presenting as a middle fossa mass (50%), posterior fossa mass (30%) or "dumbbell" tumour (20%). Malignant trigeminal schwannomas are exceedingly rare and there have only been 8 published cases in the English literature.

A previously healthy 79-year-old woman presented with a six-week history of right facial pain, headache, nausea, vomiting, gait unsteadiness and right hand clumsiness. Initial examination revealed right hand dysmetria and mild gait ataxia. Cranial CT demonstrated a 3 cm extra-axial tumour projecting from the posterior aspect of the right petrous ridge towards the cerebellopontine angle. Gross total excision was achieved via a lateral suboccipital craniectomy under brain-stem auditory evoked potential monitoring. The tumour was grossly adherent to, but separable from the trigeminal root. She was discharged home with no new deficits and complete preservation of cranial nerve function. A pathological diagnosis of malignant epithelioid trigeminal schwannoma was based on light microscopy and immunohistochemistry.

Five months later, she returned with radicular thoracic pain and spastic paraparesis. Magnetic resonance imaging (MRI) confirmed extradural tumour at T45. The original operative site was clear of disease. She received 20 Gy local irradiation in five fractions from T2-T7 and regained full strength in the legs with only mild residual hypertonia. She is alive, well, fully ambulatory and free of deficit at eighteen month follow-up. Another MRI has shown no evidence of residual cranial or spinal disease.

The clinical, radiological, surgical and pathological features of this unusual tumour variant will be presented.

P29.

Photodynamic Therapy of Recurrent Malignant Gliomas: Results of Treatment

P.J. MULLER and B.C. WILSON (Toronto; Hamilton, Ontario)

Of the 63 patients whom we we have treated with PDT 36 had recurrent malignant gliomas. These patients came to palliative reoperation and received intraoperative PDT by the balloon irradiate technique previously reported. There were 17 patients with glioblastomas [GBM], 13 with high grade astrocytoma and 6 with non-GBM malignant gliomas. The mean age and Karnofsky score was 41 and 75, respectively.

Patients received Photofrin 2 mg/kg 18-24 hours prior to surgery and photoillumination. The photic energy administered ranged from 440 to 4500 Joules [median = 1835 J] with a cavitary energy density ranging from 8.0 to 110 J/cm^2 [median = 40 J/cm^2].

The median survival of the PDT treatment group of recurrent glioma patients was 38 weeks with a %1 and %2 year survival of 32 and 15%, respectively. The median survival of the PDT treated patients with recurrent astrocytic high grade tumours was 29 weeks with a %1 and %2 year survival rate of 25% and 10%.

A retrospective review of patients with high grade astrocytic tumours [GBM and MA] treated at our institution with 2cd surgery [n = 53] with or without postoperative non-PDT treatments revealed

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a median survival of 30 weeks with a %1 and %2 year survival of 30 and 10%, respectively.

A retrospective review of patients with high grade astrocytic tumours [GBM and MA] treated at our institution revealed a median survival of 24 weeks with a %1-year and %2-year rates of 26 and 10%, respectively, after last surgery [n = 45] with or without postoperative non-PDT treatments. Survival after last surgery [n = 35] with no further radiation therapy was 17 weeks with a %1-year and %2-year rates of 22 and 0%, respectively.

These data suggest that PDT induced local tumour control may increase survival in patients with malignant gliomas.

P30.

Radioimmunolocalisation of Malignants Gliomas Using 123I-Labelled Human Monoclonal Antibodies–Phase I Study

M. DAN, G.B. PRICE, R. LISBONNA, R.J. FLANAGAN and J.G. VILLEMURE (Montreal, Quebec)

Although conventional imaging modalities (C.T., M.R.) are highly sensitive tools for detecting most malignant gliomas, situations may arise in which it may be difficult to differentiate between radiation necrosis and tumour recurrence, or estimate the extent of residual tumour following a resection, for example. We have previously reported the development of 5 stable human anti-glioma monoclonal antibodies (mAbs) of IgM isotype which appear to label cell surface glycolipids of cultured human glioma cells, but which fail to react with normal human astrocytes. In the present study, we sought to determine whether 123I-labelled human IgMmAs could be used to image high grade gliomas with sufficient specificity and low toxicity to be of clinical value. Two patients with histologically confirmed high grade gliomas, previously operated and irradiated were selected. Both patients demonstrated either recurrence or progression of their tumour on recent contrast-enhanced CT scan. The first phase of the study consisted in assessing the distribution of radioiodinated serum albumin, in order to obtain control information regarding local breakdown of the blood brain barrier and other non specific factors in the region of the tumour. In the second phase, 123I-labelled human mAb was administered i.v. and imaging carried out. Throughout the study, various clinical parameters were measured to ascertain whether any untoward toxicity occurred. Examples will be presented illustrating the results obtained.

P31.

Pediatric Cranial and Spinal Irradiation as a Predisposing Factor to Development of Meningiomas in Adulthood.

G. HADDAD, R. POKRUPA and G. BERTRAND (Montreal, Quebec)

Pediatric cranial irradiation is now recognized as a predisposing factor in the development of intracranial meningiomas in adulthood. These are recognized most commonly in countries where scalp irradiation for benign lesions was prevalent. We report seven cases of post-radiation meningiomas treated from 1987-90 at the Montreal Neurological Institute demonstrating that this is *not* a rare entity in Canada.

In this series of three women and four men, six patients had intracranial meningiomas and one has an intraspinal meningioma. One case displayed multiple meningiomas. Four were irradiated likely by the Adamson-Kienbäck technique in Europe, Israel and Morocco. 2 received Cobalt irradiation. Reasons for irradiation were: tinea capitis (3) birth mark (1), enlarged tonsils (1) and astrocytomas (2). The mean age at time of irradiation was 6 years (range 1-11 years) and of tumour diagnosis was 47 years. The average duration between irradiation and diagnosis of the meningioma was 41 years (range of 16-60 years). All cranial cases displayed radiation-induced atrophic features in all or part of the scalp, most marked in those cases treated for tinea capitis. Tumours were based in the irradiated regions in all cases of low Kv irradiation and at the edges of irradiated fields for megavolt irradiation.

A unique case of spinal meningioma was associated with MRI evident fatty changes of the vertebral bodies in the radiation portal.

A comparison between our series and the other series is provided with emphasis on the demographic and pathologic data.

P32.

Radiographic Diagnosis and Stereotactic Biopsy in Planning Therapy for Intracranial Mass Lesions

M. FURER and M. WEST (Winnipeg, Manitoba)

The diagnostic accuracy of stereotactic biopsy and the low morbidity and mortality of this procedure have been well documented. There remains, however, some question as to the need for stereotactic biopsy. Seventy consecutive cases of stereotactic biopsy were prospectively studied to determine: (1) the accuracy of radiographic diagnosis and the subsequent need for biopsy, and (2) whether the diagnosis obtained by stereotactic biopsy significantly affected the choice of therapy. Fifty-six percent of the patients were male and mean age was 50 years. Radiographic diagnoses were found to be accurate in 20% of cases. However, only cysts and cystic tumours were always correctly diagnosed radiographically. Glioblastomas and low grade astrocytomas, for example, were correctly diagnosed only half of the time. Seven percent of the biopsies were non-diagnostic. In the remaining cases, stereotactic biopsy provided information which influenced the choice of subsequent treatment. A completely unexpected diagnosis was made in 10% of cases. In 30%, the final diagnosis was considered in the initial list of differential diagnoses but confirmation by biopsy was necessary to guide therapy. In 33% of cases, the patients would have received radiotherapy regardless of the final diagnosis, but the biopsy results affected radiation dosimetry. In this series, intracranial mass lesions, excluding perhaps cystic tumours, were not reliably diagnosed by radiographic assessment alone. Stereotactic biopsy was clearly useful in providing a diagnosis and planning subsequent therapy in at least 73% of the cases reviewed. These findings suggest that therapeutic regimes for intracranial mass lesions should not be planned on the basis of radiographic assessment alone. Stereotactic biopsy to obtain an accurate tissue diagnosis is therefore justified.

P33.

Supratentorial Glioblastoma with Intramedullary Spinal Cord Glioblastoma: Metastatic or Multicentric?

M.G. HAMILTON, B.I. TRANMER and N.A. HAGEN (Calgary, Alberta)

Leptomeningeal metastasis occurs in a significant minority of patients with supratentorial malignant glioma, whereas intramedullary spinal cord metastasis is very uncommon. The appearance of symptoms referable to an intrinsic cord lesion in a patient treated for supratentorial glioblastoma (GBM) presents a diagnostic challenge, and raises questions concerning the biology of such a tumour.

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Case presentation: A 70-year-old right-handed man underwent subtotal resection of a right frontal GBM in August 1989; CT scans following conventional radiation therapy (RT) were negative for tumour recurrence. Ten months later, he presented with a 3-week history of progressive weakness and numbness of the legs, bladder difficulty and headache. Physical examination was consistent with a cauda equina or conus syndrome. Cerebrospinal fluid analysis (CSF) demonstrated markedly elevated protein, but enhanced CT head and CSF cytology x 2 were negative. A thoracolumbar myelogram was negative. An MRI scan demonstrated an intrinsic cord lesion at T10-11. At operation, the cord was distended but otherwise appeared normal. Biopsy of the spinal cord revealed GBM and was similar in appearance to the supratentorial tumour. Arachnoid biopsy was negative. He deteriorated despite spinal RT; he developed hydrocephalus, and ultimately, sepsis. Autopsy was refused.

Although it is possible that this patient suffered from multicentric glioma, we suspect the cord tumour was metastatic. We speculate that the intramedullary tumour originated from leptomeningeal deposits which caused the hydrocephalus and elevated CSF protein, even though not evident at surgery, by meningeal biopsy or by CSF cytology. Spinal cord symptoms in a patient with supratentorial glioma should prompt investigation for co-existent intramedullary tumour.

D. Pediatric Neurology

P34.

Nintendo Epilepsy: Super Mario Seizures?

M. JAVIDAN and D.B. SINCLAIR (Edmonton, Alberta)

Nintendo epilepsy has been recently described in the literature. The initial case described a 13-year-old boy who developed a generalized seizure while playing the computer game Nintendo.

We present two additional cases of previously healthy children who developed their first generalized tonic-clinic seizure while playing the Nintendo game "Super Mario Brothers III". This occurred during changes in levels of the game when extraordinary flashing bright lights appear on the screen. Neither patient experienced seizures with other computer games. The family history was negative for epilepsy in both cases and neurological examinations were normal. Electroencephalography was abnormal in both patients and revealed a photoconvulsive response during intermittent photic stimulation at flicker frequencies of 10 Hz to 20 Hz.

Nintendo epilepsy represents an unusual form of photosensitive epilepsy. The occurrence of seizures in our patients only during the "Super Mario Brothers III" games are implicated. Rather, computer games with flash components with specific photic frequencies in predisposed individuals are responsible.

P35.

Electrical Status Epilepticus During Slow Wave Sleep (ESES)

S.S. SESHIA, J. PATRICK and P.B. JAYAKAR (Winnipeg, Manitoba; Miami, U.S.A.)

ESES is primarily an EEG defined syndrome characterized by the occurrence of spike-and-slow waves (SW) continuously during non-REM sleep, the abnormalities being strikingly less frequent during the awake state and REM sleep. The case report that follows is prompted by the scarcity of communications from North America and the serendipitous documentation of the EEG evolution.

This child was seen at the age of 7 years because of developmental delay and blank spells. The DQ was 65 and she had minimal inco-ordination. A conventional EEG (CEEG) during the awake state showed SW complexes over both temporo-occipital areas. A 24-hour four channel cassette ambulatory EEG (AEEG) showed 5 and 6 discrete SW paroxysms in awake and sleep states respectively. She was treated with valproic acid (VPA). Clinically, she became seizure-free. A second AEEG at nine years of age was characteristic of ESES. VPA was discontinued at the age of 10 years. Blank spells recurred at the age of 12 years. In addition, there was regression in cognitive function. A CEEG done during the awake and drowsy states showed "non-specific" epileptiform abnormalities but another AEEG was again typical for ESES. Treatment with VPA was reinstituted but the EEG pattern has not been influenced.

A number of ascertainment biases and other factors, including the failure to obtain an adequate period of EEG recording during sleep, may contribute to the paucity of reported cases from North America compared to the frequency from Europe and Japan.

P36.

Cerebral Infarction In Children: Ten Year Retrospective Review of Winnipeg Experience

C. ADAMS, F.A. BOOTH, A.C. PATTON and S.S. SESHIA (Winnipeg, Manitoba)

Twenty children admitted to Winnipeg Children's Hospital with cerebral infarction between 1981 and 1990 are reviewed. Children with tumours, meningitis, encephalitis, head injury, or a prolonged seizure as a cause of cerebral infarction were excluded. Age range was 11 months to 17 years (mean 8.1 years with SD 5.9 years). Eleven had right hemiparesis, 8 had left hemiparesis and one had transient visual deficits. Three were dysphasic and 2 had reduced level of consciousness. Investigation included: head CT scan in all; cerebral angiogram in 15; echocardiogram in 15; PT, PTT, Protein C, Protein S, Anti thrombin III in 13; anticardiolipin antibody (Ab) in 6; ESR, C3, C4, ANF, Anti DNA Ab, Rh F in 10; cholesterol and triglyceride profile in 9; plasma amino acids in 9, and lumbar puncture in 8. Finding an etiology was the usual reason for not pursuing all investigations. Head CT scan showed areas of attenuation in the internal capsule or basal ganglia in 11, in the thalamus in 1 and in the cortex in 8. Associated with infarction were: stenosis proximal to the carotid artery bifurcation in one; hemoglobin of 47 and thrombosis of the straight sinus in 1; anticardiolipin Ab in 1; congenital heart disease and catheterisation in 1; post-op ASD repair in 1; subacute bacterial endocarditis in 1; hypertension due to 11 beta hydroxy steroid deficiency in 1; paroxysmal atrial tachycardia with heart failure in 1; Moya Moya vessels in 1; anemia with Hb 68 in 1; moderate mitral valve prolapse in 1; hemolytic uremic syndrome in 1; oral contraceptive use in 1. Duration of follow-up ranged from discharge until 3 years (mean 8.5 months, SD 9.5). At follow-up, 4 were normal, 11 had minimal deficit and 5 had moderate deficit. It is important to consider the varying etiologies in childhood cerebral infarction with investigations as outlined.

P37.

Glutaric Aciduria Type I In A Canadian Indian Child

F.A. BOOTH, W.C. HALLIDAY, B. MCCLARTY and S. PHILLIPS (Winnipeg, Manitoba)

This report details the clinical, neuroradiological and pathological findings in a Native Child with Glutaric Aciduria Type I, one of

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a group of fourteen Manitoba and Ontario Saulteaux/Ojibway Indians so diagnosed (in Press). She presented at the age of 6 months with developmental delay and was severely handicapped with increased limb tone, dystonic movements, mental retardation and seizures. She died unexpectedly at age 7.5 years. Glutaryl-COA dehydrogenase activity in lymphocytes was 9% of control. She did not consistently excrete abnormal amounts of glutaric acid or glutaric acid metabolites. Her CT Scan showed "foreshortened temporal lobes" and apparent "straightening" of the internal capsule. At autopsy, the head circumference was 52 cm. (50th%); the brain weighed 1300 gms and its external examination was normal. Coronal slices showed severe atrophy of the putamen and caudate. Light microscopy revealed the brain to be congested and edematous. The cerebellum, thalamus, brainstem, spinal cord, and globus pallidus were histologically unremarkable. The putamen and lateral caudate showed severe neuronal loss and gliosis; the medial caudate was relatively spared. The grossly normal liver, on microscopy, showed "oncocytic" changes. The kidneys, skeletal and cardiac muscle did not show any fatty change. The neuropathology is similar to that seen in previous cases with no residual enzyme activity and excretion of large amounts of glutaric acid. This suggests that either the threshold for neurological damage is low or another, as yet unclear, mechanism is operative.

P38.

Characteristics of Dysphagia in Childhood

W.J. LOGAN and J. VOROS (Toronto, Ontario)

Characteristics of dysphagia in pediatric population were surveyed retrospectively. One hundred and forty-one children who presented with swallowing difficulty of neurologic origin were included in this study. The most frequent etiology was hypoxic-ischemic encephalopathy at birth or of postnatal causes. Other etiologies were intraventricular haemorrhage, meningitis, CNS dysgenesis, cerebral infarction or haemorrhage, congenital infection, trauma, neurodegenerative disorders, neuromuscular disorder, specific mental retardation syndromes, non-specific mental retardation or developmental delay. The onset in this series varied from birth to adolescence. Aspiration pneumonia was frequent, and gastro-eosophageal reflux was usually present. By-pass feeding was required in ninety-five patients. While this improved the nutritional intake, many cases continued to have reflux and/or aspiration, and required surgical fundoplication.

We can conclude, that the common complaint of dysphagia has a variety of neurological causes. Many of these patients do not do well even after by-pass feeding. It is clear that new therapeutic strategies must be developed to manage dysphagia in childhood.

P39.

Antemortem Diagnosis of Canavan's Disease: Implications for Prenatal Diagnosis

K.J. GOULDEN, E.J. IVES and G.M. RONEN (St. John's, Newfoundland)

A male infant presented at age 2 months with unusual jerky nystagmus and was diagnosed at age 5 months with white matter degeneration and macrocephaly of unknown etiology. Brain biopsy was not done because there was no specific treatment available for any of the possible diseases. At age 4 years urine was tested for organic acids and N-acetyl aspartic aciduria was detected. N-acetyl aspartoacylase deficiency was demonstrated in cultured fibroblasts by Dr. Reuben Matalon, who has reported this enzyme deficiency as the cause of Canavan's Disease.

The child remained at a very low level of function until death from bronchopneumonia at age 5 years. Postmortem examination confirmed spongy degeneration of the brain of the Van Bogaert-Bertrand-Canavan type.

The parents had previously indicated reluctance to undertake further pregnancies because of the 25% recurrence risk (their carrier status had been confirmed on skin fibroblast culture). The mother did become pregnant, and normal fetal N-acetyl aspartoacylase levels were determined both by chorionic villus sampling and on amniocentesis (again courtesy of Dr. R. Matalon). She delivered a clinically normal female infant who remains well.

Canavan's Disease can be diagnosed both antemortem by non-invasive means and antenatally using standard prenatal diagnostic techniques.

P40.

A Probable Mitochondrial Disorder with Heteroplasmia Presenting in Siblings

D.A. ADAMS, G.M. RONEN and K.J. GOULDEN (St. John's, Newfoundland)

We describe two half-siblings with a probable mitochondrial disorder, presenting in infancy. They share the same mother, but all three parents are distantly related. The male presented with failure to thrive, developmental delay (predominantly gross motor), hypotonia, microcephaly, skeletal abnormalities, low serum carnitine, lipid laden muscle and organic aciduria.

He died at age 11 months from bilateral pneumonia and sepsis complicating neuromuscular weakness.

His younger half-sister presented at age 6 months with developmental delay (predominantly gross motor), hypotonia, microcephaly, minor skeletal abnormalities and elevated liver enzymes. The latter improved with carnitine therapy in the presence of normal free carnitine levels. Her liver biopsy showed elevated lipid with normal architecture. Muscle biopsy showed extensive atrophy and diffuse endomysial fibrosis with no abnormal deposits. She died a respiratory death at age 20 months following a progressive respiratory deterioration on a neuromuscular basis.

We feel these patients have a mitochondrial disorder in view of the following features: the probable maternal inheritance, phenotypic features and biochemical improvement of liver function tests with carnitine therapy. Neither sibling fits a clinical or biochemical diagnosis of any known mitochondrial disorder, and the differences between these half-siblings are almost as striking as their similarity. This would fit with the known heteroplasmia of mitochondrial disorders and underscores the difficulty in classifying new mitochondrial diseases.

P41.

Parental Characteristics Influencing Parenting Stress With Developmentally Delayed Infants

D.L. MACGREGOR, E. THOMPSON, S. MARCOVITCH and S. GOLDBERG (Toronto, Ontario)

A growing role of professionals in behavioral neurology is to guide families of children with identified delays to effective early intervention (EI). This study examined the relationship between parent characteristics and parenting stress as experienced by parents of infants with identified delays. Thirty-seven families, with chil-

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dren from four diagnostic groups: 1) Down's syndrome, 2) diagnosed neurological disorder (e.g. cerebral palsy), 3) prematurity, 4) developmental delays of unknown etiology, were assessed before and after 6 months of EI. Mothers completed the Parenting Stress Index (PSI) and measures of self esteem, parental locus of control and personal locus of control. Results from multivariate analyses indicated the degree to which these parent characteristics were predictive of parenting stress. Maternal self-esteem did not change over the six months of EI, but was found to predict parenting stress ($p < .001$) at both times. Mothers with higher self-esteem were experiencing less stress both before and after EI. A more 'external' parenting locus of control was correlated with greater parenting stress ($p < .001$). These results suggest that child neurologists and other professionals working with families of young developmentally disabled children need to be aware of individual differences in parent characteristics that impact on a family's success in coping with their child's difficulties.

P42.

Mental Retardation in Siblings Exposed to Bromocriptine Throughout Intrauterine Life

E.A. MACDONALD (Kingston, Ontario)

Two siblings, whose 28-year-old mother had taken oral bromocriptine for hyperprolactinemia since age 17, were seen for management of epilepsy and mental retardation. The first child, a boy, born small for gestational age, developed seizures at 4 months. The seizures were generalized and difficult to control. At 5 1/2 years he is moderately mentally retarded, with attention-deficit disorder, epilepsy, growth retardation and mild cerebral palsy. EEG shows frequent, generalized spike wave bursts. Chromosomes, CT scan of the head and biochemical investigations are normal. The second child, a girl, was growth retarded at birth, developed generalized seizures at 4 months and was treated with multiple anticonvulsants. At 3 1/2 years she is developmentally delayed, growth retarded, mildly hypertonic and has epilepsy. There are no other siblings.

The mother developed galactorrhea at age 17 and was found to have a pituitary adenoma. The literature on bromocriptine exposure during pregnancy suggests that it has no teratogenic effect, however in large series the majority of cases exposure was restricted to the first trimester. The cases described suggest the need for further studies of children exposed to bromocriptine throughout intra-uterine life.

P43.

Intraoperative EMG Monitoring for Selective Functional Posterior Rhizotomies in the Management of Spasticity

P. STEINBOK, R. KEYES, D. COCHRANE and L. LANGILL (Vancouver, British Columbia)

Selective lumbo-sacral functional posterior rhizotomies for treatment of spasticity in children with cerebral palsy is performed in many institutions, but the electrophysiologic basis of the procedure is not well understood. This report details the change in the electrophysiologic criteria used during the rhizotomy procedure as experience has been gained during over 60 cases in a single institution.

Initially, selection of nerve rootlets to be sectioned was based on a low threshold of the response to a single stimulus, and the presence of a sustained response to a 50 Hz tetanic stimulation, as described by Peacock et al. However, when posterior lumbosacral roots were stimulated in three children without spasticity, low thresholds to single stimuli and a sustained response to tetanic stimulation were sometimes observed. Whereas the response to tetanic stimulation often spread to the opposite lower limb in the spastic children, this was never seen in the three non-spastic children.

Thus, it was felt that the extent of spread might be more indicative of an abnormal rootlet than the parameters used previously. Currently, a 17 channel EEG machine is used with surface electrodes on the proximal and distal muscles of upper and lower limbs bilaterally, and the face unilaterally. The stimulation is performed as previously, and with unilateral lumbo-sacral posterior rootlet tetanic stimulation, spread of the response to the contralateral lower limb, upper limbs and even face has been noted. The extent of spread is now used as the major criterion for selection of the parts of the nerve roots to be sectioned.

The documented spread of the response into the upper part of the body has provided an electrophysiologic explanation for the improvements that have been noted in many patients at levels of the central nervous system above the lumbo-sacral rhizotomies.

P44.

Nocturnal Paroxysmal Dystonia In A Child With Progressive Spastic Ataxia

M.B. CONNOLLY, K. FARRELL and H.G.H. DUNN (Vancouver, British Columbia)

Paroxysmal episodes of dystonia which occur at night were described first in 1981 (Lugaresi and Cirignotta). Two types have been distinguished on the basis of clinical features, duration of episodes and response to antiepileptic medication. Episodes which are brief, often less than 1 minute, occur usually on arousal, respond to antiepileptic medication, and may be epileptic in origin. Prolonged episodes of nocturnal paroxysmal dystonia do not respond to antiepileptic medication, and the etiology is unknown. We describe a 10-year-old girl with slowly progressive cerebellar ataxia and spasticity, who developed prolonged dystonic episodes during sleep.

The pregnancy and delivery were normal. The older brother had a learning disability. Her gross and fine motor development were delayed and tremor and ataxia were recognized at two years of age. She developed progressive spasticity and ataxia and, at 10 years, she had head titubation, pendular nytagmus, slurred speech, hand tremor, ataxia and spasticity. There was no evidence of optic atrophy, peripheral neuropathy, scoliosis or pes cavus.

Episodes of abnormal movements during sleep started at nine years of age. Two episodes recorded during video-EEG monitoring were characterized by eyelid fluttering and asymmetric dystonic movements of her head and arms lasting 15 to 30 minutes. The EEG showed no epileptiform discharges.

Serial CT head scans were normal and T1 weighted MR images showed areas of signal attenuation in the brainstem and cervical cord. Electroretinogram was normal and visual evoked potentials showed delayed response to monocular pattern reversal stimulation. Brain stem auditory evoked responses showed a delay in Wave 5 bilaterally. Peripheral nerve conduction studies were normal. Serum immunoglobulins, cholesterol, triglycerides, alphafetoprotein, caeruloplasmin, hexoseaminidase, arylsulphatase A, lactate, and urinary alanine and oliogosaccarides were normal. The CSF protein, lactate and electrophoresis were normal. Muscle histology showed excessive variation of size in Type 1 and 2 fibres. Pyruvate carboxylase and dehydrogenase activities in skin fibroblasts were normal.

Prolonged episodes of paroxysmal nocturnal dystonia have been described in a patient who developed Huntington's chorea and in

one who did not develop other neurological problems. This is the first report of paroxysmal nocturnal dystonia in a child with progressive spastic ataxia.

P45.

Recurrent Status Epilepticus Associated With the Chronic Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

M.B. CONNOLLY, K. FARRELL and A. HILL (Vancouver, British Columbia)

Chronic SIADH occurs rarely in childhood and is associated with congenital anomalies and tumours of the central nervous system. We describe a girl of two years of age with chronic idiopathic SIADH who presented with two episodes of status epilepticus associated with hyponatraemia.

Pregnancy and delivery were normal. The birthweight was 2.2 kg. Development was normal and there was no history of hypoglycemia, dehydration, polydipsia, temperature instability or appetite disturbance. At 15 months of age, the patient had a generalized tonic-clonic seizure lasting 50 minutes. She was febrile, had a urinary tract infection, and her serum sodium was 129 mmol/L (normal 135-145). An electroencephalogram was normal. At 20 months of age, she had a second generalized tonic-clonic seizure which lasted 30 minutes and was not associated with fever. Head circumference was 46cms (-1SD), height 89cms (+2SD), and weight 11.5kg (+2SD). There was hypertelorism, and non-pitting edema of the hands and feet. The neurological examination was normal.

Laboratory investigations included: serum sodium - 119 mmol/L, urea - 1.2 mmol/L, potassium - 3.5 mmol/L, serum osmolality - 262 mosmol/kg, urinary sodium less than 5 mmol/L. Serum calcium, magnesium, glucose, albumin, liver enzymes, cholesterol and triglycerides were normal. Thyroid function and cortisol were normal. MRI and CT head scans were normal. Renal ultrasound demonstrated a duplex collecting system on the left side.

During her hospital stay, the serum sodium ranged from 119 to 132 mmol/L on regular fluid intake. With fluid restriction to 60 to 80 percent of maintenance, the serum sodium has remained within the normal range. Attempts at liberalizing fluid intake have resulted in hyponatremia. Thus, one year after diagnosis, she continues on fluid restriction. There have been no further seizures and the EEG remains normal.

This patient with chronic SIADH presented with two episodes of status epilepticus associated with hyponatremia. The fever and infection may also have been precipitating factors in the first episode but the hyponatremia was probably the major etiologic factor in both episodes. Although chronic SIADH is uncommon in childhood, this diagnosis should be considered in seizures associated with hyponatremia.

P46.

Friedreich's Ataxia and Hypomelanosis of Ito

M.B. CONNOLLY, E.H. ROLAND and A. HILL (Vancouver, British Columbia)

Friedreich's ataxia is usually inherited in an autosomal recessive fashion. Occasionally, in the late onset form, it is autosomal dominant. The gene locus for this disorder has been identified on the centromere of chromosome 9. Although most cases of Hypomelanosis of Ito are considered sporadic, autosomal dominant inheritance has been suggested (Hauschild 1982). We report a 20-year-old man with clinical features of both Friedreich's ataxia and cutaneous lesions suggestive of Hypomelanosis of Ito.

The patient was born following an uncomplicated pregnancy and delivery. Mild dysmorphic features were noted at birth including a left clubbed foot. He had mild pulmonary stenosis which did not require treatment. There was delayed development, poor coordination and learning disabilities. At age 17 years, the patient developed marked hand tremor and deterioration in his ability to write. There was no family history of Friedreich's ataxia or other neurological disease.

On examination at 18 years of age, the head circumference was 55 cm (25%). He had hypertelorism, malar hypoplasia and a high arched palate. There was bilateral pes cavus and a left clubbed foot. On the shin, there were multiple large hypopigmented macules. There were also irregular areas of whorled pigmentation with midline demarcation. There was generalized freckling on the abdomen. Cranial nerve examination was normal. There was decreased muscle bulk in the left lower leg. The deep tendon reflexes were brisk at the knees bilaterally and the ankle reflexes were absent. The plantar responses were upgoing. The gait was ataxic. There was decreased vibration and position sense in both lower limbs.

Investigations revealed the following: nerve conduction studies indicated peripheral sensory and motor neuropathy (lower limbs more than upper limbs). There were mixed axonal and demyelinative features and abnormal F responses in the left leg. The electroencephalogram and computed tomography scan of the head were normal. Chromosome karoyotype was normal. Cytogenetic analysis of cultured skin fibroblasts demonstrated a normal male karyotype. Immunoglobulins, cholesterol, triglycerides, lactate, very long chain fatty acids, ceruloplasmin and hexosaminidase were normal.

This patient has an unusual combination of both Friedreich's Ataxia and Hypomelanosis of Ito which raises the possibility of a genetic linkage between these two disorders.

P47.

Cerebral Fluid Cholinesterases Levels in Neonates with Neurologic Disorders

G.M. RONEN, D. TERESPOLSKI, K.M. KUTTY and D.G. BRYANT (St. John's, Newfoundland; Halifax, Nova Scotia)

The cerebrospinal fluid (CSF) contains the enzymes acetylcholinesterase (AChE) and pseudocholinesterase (PChE). The former is of neuronal and the latter of glial origin. We raise the question of whether CSF cholinesterases levels correlate with different types of neonatal CNS disorders and their severity. If so, one may be able to use them in the clinical setting, e.g. as an assessment of the degree of neonatal brain injury. We therefore undertook a pilot study to evaluate the potential diagnostic value of CSF cholinesterases levels in neonates with neurologic disorders.

CSF cholinesterase levels were assessed in 31 neonates (10 with hydrocephalus, 5 with hypoxic ischemic encephalopathy (HIE), 10 with seizures of other causes and 5 without detectable CNS abnormalities). One case was excluded due to CSF xanthochromia with very high PChE levels. The CSF was collected from the lateral ventricle during the shunting procedure in 9 and from the open myelomeningocele in 1 - hydrocephalic patients; and through a lumbar puncture in all others.

Using the Kruskal-Wallis analysis of ranks the hydrocephalus group had the highest ($P < 0.10$) AChE levels 31 ± 21 IU/L (mean $\pm$ SD); HIE 18 ± 6; seizure group 17 ± 8; and non CNS abnormalities 14 ± 4. The PChE average levels were also highest ($P < 0.05$) in the hydrocephalus group 25 ± 13; and, equal in the

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other groups HIE 11 ± 6; seizure group 12 ± 6; and non CNS abnormalities 9 ± 1. Individual results within groups were very variable and clinical correlation require further analysis and/or bigger samples.

We conclude that neonates with hydrocephalus possibly have the highest levels of AChE and most probably of PChE. Neonates with other neurologic disorders could not be simply grouped in a way which shows clear distinction on AChE/PChE levels.

This test might be of use in specific settings, however this will require further assessment.

P48.

Familial Basal Ganglia Calcifications: A Congenital Infection, Fahr's Disease in Infancy of a Non Progressive Encephalopathy?

P. DIADORI, H.Z. DARWISH, R. AUER and B. FOWLOW (Calgary, Alberta)

The presence of cerebral calcifications in infancy always raises the issue of whether the infant was exposed to in utero infection. Calcification of the basal ganglia in particular has been associated with hypoparathyroidism and other disorders. One form of Fahr's disease has an autosomal dominant pattern of inheritance and is asymptomatic in childhood. Aicardi & Gauttiere (Ann Neurol, 1984) described a familial progressive encephalopathy with CSF lymphocytosis. In this report we describe an unfortunate family in which three siblings have demonstrated evidence of a CNS inflammatory response, two of whom have cerebral calcifications and a *non* progressive encephalopathy.

The first born female sibling died suddenly in her sleep at 6 months without prior abnormality. Autopsy revealed dramatic perivascular monocytic infiltrates of the brainstem region. There was minimal calcification of the cerebral vessels in the basal ganglia. A systematic search for an infectious etiology which included examination for antigens and viral particles was negative. A 25-month-old live male sibling has truncal hypotonia and appendicular hypertonia and his 6-month-old brother has generalized hypertonia, and both have moderate global delay, but continue to gain skills. CSF showed mild lymphocytosis. Torch and viral titres are negative. CT scan shows punctate bilateral calcifications (30-70 HU) in the lentiform and thalamic nuclei. NMR in addition shows deposition of iron pigment and bilateral hemispheric demyelinating lesions.

Since no "infectious" etiology could be defined these findings may suggest a process akin to autoimmune response triggered in utero or soon after birth. Because of the delayed development and CSF lymphocytosis we are considering treatment with corticosteroids.

P49.

Brain Abscess in Children Secondary to Esophageal Dilatation

HILDA ALCALA, JOSE CORNELIO, GUILLERMO DAVILA, ALFONSO ESCANERO and CECILIO BELIO (Mexico, D.F., Mexico)

Brain abscess secondary to esophageal dilatation due to caustic stenosis has been reported in the literature since 1973 in adults. In children it has been reported in 5 instances as individual cases. This paper reports 4 children who developed brain abscess in the process of esophageal dilatations. There were three boys and one girl; ages ranged from 4 to 6 years. Clinical presentation was that of fever, focal signs and increased intracranial pressure of sudden onset. Diagnosis was suspected clinically and confirmed by CT of brain in all. Location of the abscess was supratentorial in three and cerebellar in one. CSF abnormalities, characteristic of brain abscess were found in only one child. All four abscesses were single. No organisms were cultured from the purulent material removed at surgery. All children were treated with antibiotics and surgical removal. All children are alive and well. The pathology involved seems to be a bacteremia caused by rupture of small vessels during dilatations, allowing intraesophageal organisms to reach the blood stream.

Pediatric neurologists should be alerted to this pathologic association in children.

E. Neuro-Imaging

P50.

MRI Measurements in 23 Members of the Family with Hereditary Ataxia

A.P. GASECKI, J.F. AITA, L. SCHUT and F. HAHN (Omaha; Minneapolis, U.S.A.)

We have studied with cranial MRI 23 members of a family with an autosomal hereditary ataxia. All family members studied either have (9 patients) or are at risk (14 patients) for Olivopontocerebellar Atrophy (OPCA).

The sagittal, T1-weighted, partial saturation, and spin-echo sequences were performed on the affected and at-risk family members. Five measurements were made: mesencephalon, pons (at midway), pontomedullary junction, medullospinal junction, and cervical spinal cord. The values were made in respect to the anteroposterior diameter of the skull to calculate ratios and prevent the data being affected by head dimensions. In addition, the ratio of the middle cerebellar peduncle to clivus diameter was determined.

We demonstrated a statistical significance (p value less than 0.05) of all six ratios in the affected by the disease group of patients as compared to the group at risk for developing OPCA. Thus, the measurements of brainstem and spinal cord diameters and ratios may become valuable and could aid in the clinical diagnosis. Atrophy of the middle cerebellar peduncle may substantiate a diagnosis of cerebellar degeneration on magnetic resonance imaging.

P51.

Magnetic Resonance C.S.F. Flow in Hydrocephalus

J.-G. VILLEMURE and D. MELANSON (Montreal, Quebec)

Magnetic Resonance in hydrocephalus offers three approaches: imaging, spectroscopy and C.S.F. flow study. The authors illustrate with video, C.S.F. flow studies in 2 control subjects and in 4 N.P.H. subjects before and after shunting.

C.S.F. flow with M.R. remains to be explored further, but offers a dynamic appreciation of C.S.F. physiology.

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P52.

Transient Focal Cortical Edema Which Mimics Pachygyria

C.P. WHITE, E. ROLAND, K. POSKITT and A. HILL (Vancouver, British Columbia)

Focal abnormalities observed on computed tomography or magnetic resonance imaging are associated with a variety of neurological disorders, e.g., tumor, infarction, cerebral dysgenesis or encephalitis. We report an 8-year-old girl who had focal enlargement of gyri which was considered initially to represent cerebral dysgenesis (pachygyria) or tumour but which resolved subsequently after several months.

The patient was an 8-year-old girl who presented with right-sided headache and low-grade fever of two days duration. One day prior to admission, she developed sudden onset of left hemiplegia. Rectal temperature was 38.6°C. She had a homonymous hemianopia, pyramidal weakness, sensory inattention and deceased graphesthesia involving the left limbs. These clinical abnormalities improved during the following two weeks.

The initial CT scan demonstrated mild effacement of sulci in the right parieto-occipital region without associated decreased tissue attenuation. Electroencephalography demonstrated continuous delta activity in that region. Magnetic resonance imaging performed six days later demonstrated localized thickening of the gyri and compression of the sulci in the right posterior parietal region. In the underlying white matter, there were patchy areas which had signal characteristics of gray matter. The remainder of the brain appeared normal. These abnormalities were considered to be most consistent with focal pachygyria and heterotopia. The following investigations were normal: coagulation screen, cerebrospinal fluid examination, blood and CSF serology for specific viruses. Repeat neurological examination and CT scan performed four months later were normal.

Transient abnormalities on CT and MRI scans, presumably due to focal edema, have been reported in association with focal seizures and encephalitis. In this patient, the absence of seizures and the duration of neurological abnormalities (>2 weeks) argues against post-ictal paresis. The combination of fever and transient focal abnormalities suggest focal encephalitis despite normal CSF examination.

This case demonstrates that focal brain swelling, on both CT and MRI is a non-specific feature which may mimic congenital migrational abnormality or tumour. Follow-up imaging studies may be necessary to determine the transient nature of the findings.

F. Multiple Sclerosis

P53.

Primary Autoantibodies to Myelin Basic Protein Purified from the Cerebrospinal Fluid of Multiple Sclerosis Patients React with Homologous and Heterologus Antigens

K.G. WARREN and I. CATZ (Edmonton, Alberta)

A myelin basic protein (MBP) antibody cascade was identified in the cerebrospinal fluid of multiple sclerosis patients. Primary autoantibodies such as anti-myelin basic protein (anti-MBP) are directed against myelin antigens. Secondary autoantibodies are capable of neutralizing primary autoantibodies and are associated with the remission phase of MS. Tertiary autoantibodies inhibit secondary autoantibodies and are associated with the chronically progressing phase of MS. Anti-MBP is present in a free/bound ratio above unity in patients in the early phase of acute relapses and below unity during the late phase of acute relapses and during the chronically progressive phase of the illness.

Primary autoantibodies to myelin basic protein (anti-MBP) were purified from the cerebrospinal fluid of multiple sclerosis patients with acute relapses by two step affinity chromatography. IgG was purified from the total proteins by Protein A Sepharose affinity chromatography. Anti-MBP was obtained from the purified IgG by antigen specific (MBP-Sepharose) affinity chromatography. Myelin basic protein was prepared from the central nervous system of homologous (humans) as well as heterologous (bovine and porcine) species. The primary autoantibodies to myelin basic protein purified from the CSF of MS patients reacted equally to human, bovine and porcine MBP. This equal immunoreactivity may be due to the similarity of MBP isolated from these three different sources. MBP from human and bovine sources are both 170 amino acids long differing in structure by thirteen residues. Human as well as bovine myelin basic protein can be used in further studies to identify the epitope(s) for these primary autoantibodies from MS patients.

P54.

Prevalence, Incidence and Family Patterns of Multiple Sclerosis (MS) in Barrhead County, Alberta, Canada

S.A. WARREN and K.G. WARREN (Edmonton, Alberta)

Klein et al (CJNS 1990; 17: 241) have reported MS prevalence rates of 87 and 202 per 100,000 respectively for Cardston and Crows Nest Pass, Alberta. To clarify which rate may be more representative, the University of Alberta MS Clinic conducted a prevalence study in Barrhead Country, which is at the geographic centre of the province.

Cases were ascertained through the files of the MS Clinic, all doctors practising in the county, the county's 1 general hospital, 1 nursing home, local public health unit and MS Society chapter. Patients were examined by the Clinic neurologist and classed as possible, probable or definite using Poser's criteria. Gender, age, onset age, place of residence at onset, and MS family history were also recorded.

Twenty patients were identified among the county's 9,720 residents. All rates were calculated per 100,000 population, with a 95% confidence interval (CI). Using only probable/definite cases (N = 19), a crude point prevalence rate of 196 (CI ± 27) was observed for January 1, 1990. The rates for males and females were 184 (±26) and 207 (±28). No cases were <25; the rates for 25-64 year olds and 65+ patients were 346 (±36) and 85 (±18). Twelve patients were living in Barrhead County at onset, giving average annual incidence rates of 1.3 (±.2) for 1950-59, 5.0 (±.4) for 1960-69, 3.8 (±.4) for 1970-79, and 4.3(±.4) for 1980-89. 40% of the cases reported an MS relative. Two patients were sisters who reported each other; none of the other patients were related, but 6 reported an MS relative living outside the area (1 mother, 3 sisters, 2 aunts, 1 great aunt, 1 niece).

Alberta's prevalence rate may be close to 200, the highest reported in Canada. Or both Crows Nest Pass and Barrhead County may be excess risk areas. The high prevalence in Barrhead County is not due to a few families with more than 1 MS member living in the area. The incidence pattern suggests a constant environmental risk factor not point epidemic.

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P55.

Pain in Multiple Sclerosis: Prevalence, Distress and Role-related Restrictions

C.J. ARCHIBALD, P.G. RITVO, J.D. FISK, P. MCGRATH and T.J. MURRAY (Halifax, Nova Scotia)

Previous studies have reported variable prevalence rates for pain in MS patients. In this study we report on data collected from the Dalhousie MS Research Unit. In this sample, the prevalence of self-reported pain in the past month was 54.5%. Subjects reported that their usual pain levels averaged 57% of the most extreme pain in their subjective experience. The median number of hours per week in which pain was experienced was 78.5. They rated their average pain-related distress levels to be 54% of the most extreme distress subjectively experienced. As a result of their pain, the subjects were able to function at only 76% of their expected levels in roles as parent, spouse, worker, friend and sportsperson. The presence of pain was not associated significantly with age, sex, disease duration, Kurtzke Disability Status Scale score, or diagnostic classification of MS (benign, relapse-remitting, relapsing-progressive, chronic progressive). Although the presence of pain is not clearly associated with specific clinical features, these data indicate that pain is widely prevalent in MS and is a significant cause of distress and role-related restriction.

G. Neuro-Ophthalmology

P56.

Wegener's Granulomatosis Presenting as External Ophthalmoplegia

M. McLEAN, C.L. BARCLAY and W.A. FLETCHER (Calgary, Alberta)

Wegener's granulomatosis is a systemic vasculitis with necrotizing granulomatous inflammation of small and medium-sized vessels. Usually it affects the upper respiratory tract first and later progresses to involve the lower respiratory tract and kidneys. Eye involvement occurs in 25-50% of patients and may include conjunctivitis, scleritis, optic neuritis, ophthalmoplegia and proptosis. The eyes are rarely the first to be involved and are never involved in isolation. We report a case where the initial manifestation was external ophthalmoplegia with no other systemic involvement.

A 48-year-old woman presented with left periorbital pain and diplopia. Visual acuity was 20/20 OD and 20/40 OS. There was swelling of the left optic disc, left proptosis and complete left external ophthalmoplegia. Over 24 hours visual acuity fell to 20/200 OS and she developed an unreactive left pupil and decreased sensation over the distribution of V1 on the left.

CT showed opacification of the ethmoid and sphenoid sinuses with erosion of the median septum and medial wall of the left orbit and infiltration of the left medial rectus and superior oblique muscles. CXR showed blunting of costophrenic angles with no parenchymal disease. Urinalysis was normal. Pathology from a biopsy of sphenoid sinus showed necrosis of mucosa and vasculitis with giant cells, diagnostic of Wegener's granulomatosis.

Treatment with prednisone and cyclophosphamide caused partial recovery of extra-ocular movement and sensation in V1 and improvement of visual acuity of 20/80 OS.

This case illustrates that Wegener's granulomatosis may present solely with eye manifestations.

P57.

Neuro-Ophthalmic Emergencies in Retrobulbar Anesthesia

A.C. ORR and C.E. MAXNER (Halifax, Nova Scotia)

Cataract extraction is one of the most frequently performed operations in North America. Although the orbital complications of the regional retrobulbar block utilized in this procedure are well recognized, potentially fatal non-allergic sequelae can occur. These have come to assume increasing importance given the trend to performing cataract extraction using local anesthesia in the outpatient setting.

Two cases referred urgently to our Neuro-Ophthalmology service are presented as examples of life-threatening risks associated with retrobulbar anesthetic usage. In the first, generalized seizures developed immediately after retrobulbar anesthetic injection and in the second, gradual loss of consciousness culminated in a respiratory arrest. We discuss proposed mechanisms for each episode and review appropriate management.

FRIDAY, JUNE 21, 1990

H. General Neurology

P58.

Periodic Lateralized Epileptiform Discharges in Multiple Sclerosis, A Case Report

S. JARJOURA and A. LAMONTAGNE (Sherbrooke, Quebec)

Periodic lateralized epileptiform discharges (PLEDS) and usually seen with an acute or subacute lesion of the cerebral hemisphere, either a vascular insult, herpes simplex encephalitis or a tumour. We present the case of a 23-year-old Caucasian woman with a two-year history of multiple sclerosis (MS) who was admitted to the hospital in status epilepticus characterized by several left partial motor seizures with secondary generalization and a transient left hemiparesis.

Computed tomography of the head showed only generalized cortical atrophy. An EEG recording obtained on arrival showed PLEDS consisting of periodic slow spikes occurring every second on the right anterior temporal region. A magnetic nuclear resonance study obtained a few months later revealed multiple periventricular lesions and foci of increased signal intensity in the right temporal lobe, suggesting a relation between the partial seizures of the patient and her demyelinating disease.

Forty per cent of patients with MS may have EEG abnormalities, mostly of a non specific nature. Two to six per cent have convulsions but very few have been described with status epilepticus and PLEDS, none to our knowledge with NMR correlation. This case illustrated that MS might be included in the differential diagnosis of PLEDS.

P59.

Paroxysmal Epileptic Dysphasia: An Unusual Presentation of Multiple Sclerosis

S.R. LAM, R.M. MOSEWICH and A. SHUAIB (Saskatoon, Saskatchewan)

Partial seizures have not previously been described as the presenting feature of multiple sclerosis. An unusual case of multiple

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sclerosis is described in which partial seizures, manifested by dysphasia, were the presenting feature.

A 45-year-old, right-handed female presented in 1981 with seizures. Previously, she had experienced episodes of comprehension difficulty and speech arrest. Neurological examination, EEG and CT scan of the brain were normal and the patient was treated with phenytoin.

More recently the frequency of these episodes increased, and she began to have frequent headaches. By 1990, she was having daily episodes. Physical examination and EEG were again normal. It was suspected that her paroxysmal symptoms were dysphasias due to partial seizures. EEG telemetry monitoring captured two bursts of focal discharges in the left parietal and temporal regions. An MRI scan of the brain showed multiple white matter lesions typical of multiple sclerosis, including lesions close to Wernicke's area. Subsequent investigations have shown elevation in CSF protein and abnormal visual evoked responses.

Although epilepsy and other paroxysmal seizures have been described in known cases of multiple sclerosis, partial seizures have not been described as a presenting feature. This case represents an unusual manifestation of partial seizures which turned out to be the presenting feature of multiple sclerosis.

P60.

International Survey of Neurologists and Epilepsy Organizations Concerning Legal Aspects of Epilepsy and Driving

G. RÉMILLARD, B. ZIFKIN and F. ANDERMANN (Montreal, Quebec)

A questionnaire was addressed to physicians attending the 1989 International Epilepsy Congress in New Delhi, India. It concerned their experience with epilepsy and driving and their views on mandatory reporting of individuals with epilepsy. We received 177 responses from 33 countries on all continents. We found that neurologists specialized in epilepsy working in different countries had similar approaches to mandatory reporting. They reported patients only in exceptional circumstances regardless of local licensing law though they were treating 100 or 1000 or more such patients in a typical year. Eighteen organizations listed by International Bureau for Epilepsy from 16 countries also replied to a questionnaire. Over 90% believed that the responsibility of the treating physician should be to make his patient aware of his duty to self-report rather than be obliged to report all epileptic patients to legal authorities. Similar responses were obtained from 48 of 59 lay groups contacted from all 10 Canadian provinces. Both physicians expert in epileptology and organizations representing epileptic people should participate in the establishment of legislation regulating legal aspects of motor vehicle driving.

P61.

MELAS Presenting with Hearing Loss, Retinitis Pigmentosa and Hypothalamic Hypogonadism

R. MOSEWICH, J.R. DONAT, A. SHUAIB, S. DiMAURO and E. CIAFALONI (Saskatoon, Saskatchewan; New York, U.S.A.)

Mitochondrial myopathy, encephalopathy, lactic acidosis, and strokelike episodes (MELAS) was described by Pavlakis and colleagues in 1984. It is one of a spectrum of diseases affecting mitochondrial function which have diverse clinical manifestations and which are characterized pathologically by ragged red fibres on muscle biopsy. Recently a tRNA mutation has been found in patients with MELAS by Goto et al (Nature (1990) 348.651).

We report a large family whose members have sensorineural hearing loss, retinitis pigmentosa, hypothalamic hypogonadism and mild myopathy. Only one member had a strokelike episode. Affected members of this family have been shown to carry the mutation described in MELAS but their syndrome does not resemble the classic MELAS syndrome.

This report emphasizes that in kindreds with undiagnosed sensorineural deafness or retinitis pigmentosa, mitochondrial myopathy should be considered in the differential diagnosis even in the absence of strokelike episodes.

P62.

The Prevalence of Dementia and Alzheimer's Disease in Cree Indians in Manitoba: A Preliminary Report

N. PILLAY, H.C. HENDRIE, K.S. HALL, D. ROGERS, C. PRINCE, J. NORTON, H. BRITTAIN, A. NATH, A. BLUE, J. KAUFERT, P. SHELTON, B. POSTL and B. OSUNTOKUN (Brandon, Manitoba; Indianapolis, U.S.A.; Nigeria)

Awareness that prevalence of dementia and its principal form, Alzheimer's disease (AD) is increasing at an alarming rate in the aged population has captured the attention of the general public and spurred the interest of investigators. In many community studies there are differences reported in prevalence rates. Investigators have interpretated the variation to different methodologies. Despite the widespread concern for Alzheimer's disease, information on the frequency and distribution of specific dementing disorders amongst the various racial and ethnic communities is either unknown or remains limited.

We developed comparative methods of screening in 2 culturally distinct populations for case identification and completed a methodological survey. We report the prevalence rates for dementia and Alzheimer's disease.

In a community survey of 198 Cree Indians aged 65 and over registered in 2 reserves in Northern Manitoba, only 1 case of probable AD was identified from 8 cases of dementia giving a prevalence rate of 0.5% for AD and 4.2% for all dementias. This contrasted with an aged-adjusted dementia in an age-stratified sample of 252 English-speaking residents of Winnipeg using the same screening instruments and the same clinical evaluation team of physicians. The difference in prevalence rates between the populations for Alzheimer's disease was highly significant ($p < .001$) but not for all dementias.

Our results indicate that AD, but not dementia, occurs less often in the Cree communities than the non-Indian population of Winnipeg. Since this was a small study of 2 total communities, extrapolation of our results to other Indian communities, even Cree speaking is limited. Even with the expressed reservations the results would suggest that expanded evaluations of other Indian communities would be worthwhile.

P63.

Diabetic Neuropathic Cachexia: An Uncommon Variant with a Benign Prognosis

N. PILLAY and A. MEHTA (Winnipeg, Manitoba)

In subjects with diabetes mellitus, the diagnosis of painful distal sensory neuropathy invariably implies a bleak future with no effec-

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tive treatment to halt progression or alleviate pain. When associated with significant weight loss, this may comprise a specific syndrome.

Two adult male patients with preexisting mild diabetes, both insulin independent presented acutely with severe burning and unremitting pain in legs and feet. Both reported a slow but progressive and profound weight loss of 49 and 29.5 kg, impotence, depression and anorexia. Moderate to severe cachexia and generalized loss of subcutaneous muscle tissue was prominent in both patients. Both had mild to moderate proximal and distal weakness. Pinprick, light touch and temperature was impaired in a stocking pattern. Vibration and joint position was intact in 1 patient and absent in the other. Deep tendon reflexes were absent and plantar responses were flexor. There was no evidence of associated diabetic retinopathy or nephropathy. Both were treated with insulin and diet and blood glucose control was established. Amitriptyline was effective for pain control. Nerve conduction velocities demonstrated axonal neuropathy.

Within 6 months, the symptoms of neuropathy subsided and depression resolved. At 2 year follow-up, one patient was asymptomatic and he had regained 32 kg considered just about his ideal and the other patient at 6 months follow-up was still improving with 18.2 kg of weight regained.

We conclude that acute painful distal diabetic neuropathy in association with substantial weight loss in our patients constitutes a distinct syndrome which was first described as diabetic neuropathic cachexia by Ellenberg (1973). Although the presentation is seemingly grave the outcome is benign. Proximal motor neuropathy also known as diabetic amyotrophy may be a variant of this syndrome.

P64.

C6 - C7 Disc Protrusion Presenting with Chest Wall Pain

M.C. YEUNG and N.A. HAGEN (Calgary, Alberta)

Herniation of a cervical intervertebral disc can occasionally be associated with a minor degree of chest wall discomfort. However, chest wall pain as a major presenting complaint of herniated cervical disc is unusual. We present 2 such cases, both of which were referred to a neurologist with the diagnosis of "possible brachial plexopathy."

A 40-year-old woman developed a sudden onset of severe right arm pain while dressing. Right shoulder, arm, and hand pain was associated with symptoms of hyperesthesia and cutaneous allodynia which extended down to the chest to about the T6 level. Physical examination revealed weakness and loss of reflexes in the right arm; there was no evidence of myelopathy. Sensory examination demonstrated hypesthesia, hyperpathia and cutaneous allodynia in a C6 to T7 distribution. Neck extension and lateral rotation made symptoms markedly worse. Myelography and CT imaging revealed a C5 - C7 right posterolateral disc herniation with effacement of the spinal cord. Surgical decompression resulted in prompt improvement of all symptoms.

A second similar patient was seen, with similar findings and a disc protrusion at the same level.

We conclude that, although unusual, chest wall pain can occur ipsilateral to a herniated C6 - C7 disc, along with the more typical C7 radicular complaints. A diagnosis of brachial plexopathy may be considered because of signs and symptoms involving more than one dermatome or root distribution. Myelographic and CT investigations revealed spinal cord compression ipsilateral to the side of the chest wall pain; we speculate that the C5 - T6 sensory complaints are spinal cord in origin.

P65.

Comparison of Flunarizine, a CNS Specific Calcium Channel Antagonist, to Propranolol in the Prophylactic Treatment of Migraine

M.J. GAWEL, J. KREEFT, R.F. NELSON and D. SIMARD (Scarborough; London; Ottawa, Ontario; Quebec City, Quebec)

This randomized, double-blind, parallel-group trial compared the safety and efficacy of 10 mg flunarizine o.d. (**SEBELIUM***) to 80 mg propranolol b.i.d. for the prophylaxis of migraine headaches. A total of 94 patients were enrolled in the trial. Five patients were excluded from the analysis leaving 44 patients randomized to flunarizine and 45 to propranolol. There was a one month placebo baseline period followed by a four month active treatment phase. Patients recorded number of migraine attacks, duration, severity and use of symptomatic relief medication in diaries. Patients were also seen for clinic visits on a monthly basis.

The results indicate that both treatments induce a significant reduction in the frequency of migraines ($P < 0.05$) but do not affect severity or duration. Treatment was also associated with a significant reduction in the concomitant use of analgesics. Globally, 67% of flunarizine patients and 51% of propranolol patients responded positively to treatment.

Flunarizine had no effect on cardiovascular function while propranolol induced significant reductions in blood pressure and heart rate. Weight gain was significant for both treatments and was more evident in the flunarizine group. However, the body mass index was found not to exceed the boundaries of normal for either treatment group.

In summary, both treatments were judged to be effective and well tolerated. Flunarizine is, therefore, a valuable addition to the therapies currently available in Canada.

P66.

Antemortem Echocardiographic Diagnosis of Non-Bacterial Thrombotic Endocaditis in a Young Woman with Stroke

R.A. PURDY, J.M. DAHMER, T.J. NEVILLE, T.J. MARRIE and C.J. KOILPILLAI (Halifax, Nova Scotia)

Non-Bacterial Thrombolic Endocarditis (NBTE) is not an uncommon finding in patients with a malignancy. However, it is rarely diagnosed antemortem since the neoplasm may be occult. Cardiac findings can be minimal and vegetations are frequently too small to be seen on transthoracic 2D echocardiography.

We present the case of a young woman with right hemisphere stroke, NBTE and occult ovarian carcinoma, in whom the diagnosis was suspected when blood cultures were negative, despite physical and echocardiographic evidence of endocarditis.

Clinical, laboratory and pathological data will be presented, along with a review of the pertinent literature and discussion of the use of echocardiography in this disorder.

P67.

Post-Traumatic Collet-Sicard Syndrome Associated with a Skull-Base Anomaly

C.E. MAXNER, B.D. BYRNE, W.S. HUESTIS, R.O. HOLNESS and T.D. LOANE (Halifax, Nova Scotia)

Trauma-induced Collet-Sicard syndrome (unilateral CN IX, X, XI, XII palsies) although rare, has been described primarily in asso-

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ciation with skull base fractures which pass through the jugular foramen and hypoglossal canal.

We report the case of a 40-year-old man who was involved in a motor vehicle accident which resulted in a right hemopneumothorax as well as multiple cranial nerve palsies. He demonstrated transiently impaired CN VI function bilaterally along with persistent left CN IX, X, XI, and XII dysfunction.

Radiographic studies including computerized tomography and magnetic resonance imaging did not reveal any skull base fracture however a congenitally anomalous bony outgrowth from the anterior lip of the foramen magnum was demonstrated. This anomalous structure compressed the right side of the medulla. It is postulated that this structural anomaly contributed to the development of his left Collet-Sicard syndrome by "tethering" the right side of the medulla, possibly exposing his left CN IX-XII to greater traumatic forces.

P68.

T. Gondii Ventriculitis in HIV Positive Patients

A. GENGE, S. CARPENTER and G. FRANCIS (Montreal, Quebec)

Toxoplasmosis is the most common cause of intracerebral mass lesions in patients with AIDS and may also cause a more diffuse encephalitis. We report the presence of a severe fatal ventriculitis due to toxoplasma gondii infection.

Three patients with HIV infection were seen with this complication between April 1986 and August 1990 at the Montreal Neurologic Institute. One patient presented with symptoms of an intracranial mass lesion, one presented with encephalopathy and the third presented with symptoms of acute hydrocephalus. All 3 patients deteriorated and died rapidly as a result of hydrocephalus and herniation.

Gross inspection at autopsy revealed the ventricles to be filled with thick pink gelatinous material impeding normal CSF circulation. Microscopic examination revealed a severe destructive inflammatory ependymitis with the presence of oocyst and tachyzoites in the periventricular white matter.

The impaired CSF flow is due to the gelatinous ventricular contents and produces hydrocephalus with eventual herniation. This entity should be considered in the clinical setting of HIV+ patients with CT/MRI evidence of ventricular enlargement.

P69.

Clinical Findings in Neuro-Brucellosis

Z. AL-KAWI, S. BOHLEGA and S. OMER (Riyadh, Saudi Arabia)

Involvement of the nervous system with brucellosis can be either in the form of acute meningitis or in a chronic form. We reported our experience with twelve cases of neuro-brucellosis. The clinical presentation may be obscure and masquerade in syndromes of polyradiculopathy, sensory neural hearing loss, multiple sclerosis like picture, transient ischemia episodes or other manifestations. MRI and CSF findings may be equally deceptive unless the diagnosis is suspected on epidemiological grounds. Chronic brucellar infection of the nervous system like syphilis is a great mimicker and should be considered in the differential diagnosis of many neurological syndromes since this is treatable with specific antibiotics.

P70.

Favorable Outcome in Cephalic Tetanus

M. THIBAULT, D. BRUNET, S. DUPRÉ and J.-P. BOUCHARD (Quebec, Quebec)

Cephalic tetanus is a rare form of tetanus. It accounts for only 1-3% of total cases reported. It is characterized by trismus and various signs of paralysis of one or more cranial nerves. The process may remain localized but becomes generalized in $^{2}/_{3}$ of the cases. Mortality ranges from 15 to 30% and is a function of the spread of the process.

A 60-year-old man presented with a subacute bulbar palsy. Ten days before he had complained of difficulty in swallowing and opening the mouth. There was no pain, fever or trauma prior the symptoms. Increasing dysphagia and hoarseness of the voice soon developed. He was intubated and later tracheotomized, but never needed mechanical ventilation. At the acme of the disease, he presented a trismus and a moderate blepharospasm (R L) without ocular muscle involvement. He barely moved the tongue and weakness of the right vocal cord was noted. There was moderate contracture of the posterior neck muscles. CT scan and MRI of the brain and brain stem were normal, as well as CSF studies. Electrophysiological studies revealed the loss of the normal silent period in the masseter muscle when the jaw reflex was elicited. EMG of facial and cervical muscles showed constant firing of numerous motor units at rest, at rates of 25-30 Hz. Motor conduction of the right median nerve was normal, but F waves were absent. He received human antitetanic immunoglobulin, penicillin and ceftriaxone. Signs increased under medication for one week, but slowly waned to normal over the next 4 weeks.

Although most of the cases of cephalic tetanus present at first with trismus and signs of trauma to the ipsilateral face, some cases present with a subacute multiple cranial nerve palsy without any sign of injury. Early recognition and management of this rare form of tetanus can limit the spread of the process so that complete recovery can occur in a few weeks.

P71.

Normal Gait: How Wide is the Stride?

G.B. YOUNG, J. KREEFT and D. WINTER (London; Waterloo, Ontario)

The distance between the feet while walking (stride width) is often used as a clinical index for ataxia of gait. This assessment is usually made in a subjective manner, without reference to established norms.

We used a simple method to assess stride width in which subjects walked barefooted over flour sprinkled on the floor. A straight line (line of progression) was drawn between left and right footprints and an average stride width was calculated from measurements of the medial border of the footprints to the line of progression. Twenty-three healthy men (aged 26-72, mean 49 years) and 18 healthy women (aged 25-82, mean 47 years) were studied.

Mean stride width for men was 6.12 (S.D. 3.14) cm and 3.62 (S.D. 2.58) for women ($p < 0.01$). There was a mild, nonsignificant increase in stride width with age for both men and women.

Thus, there is considerable variation in stride width in the normal population and males and females differ significantly. Clinicians should take this into consideration when they inspect the gait of their patients.

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P72.

Finger Tapping and Cardiac-Locomotor Coupling

R.L. KIRBY, S.E. CARR and D.A. MACLEOD (Halifax, Nova Scotia; Toronto, Ontario)

Finger tapping is a task that has been widely used to study coordination, including the effects of handedness, gender, competing tasks, anxiety, drugs, aging and neuropathology. Coupling between cardiac and locomotor rhythms has been identified while people walk, run, hop and cycle at cadences natural to them. The object of this study was to test the hypothesis that cardiac-locomotor coupling occurs during finger tapping, to provide insights into both the control of finger tapping and the mechanisms underlying cardiac-locomotor coupling. We studied 20 normal subjects tapping a telegraph key at a comfortable rate for 10 min. Fifteen subjects (75%) coupled significantly at one or more single-digit integer ratio (heart/tapping rate), the most common of which was 1:2. Coupling at particular ratios appeared to be "clustered" over time. All subjects reported some fatigue and loss of fine dexterity towards the end of the protocol. Such coupling should be considered a potentially confounding variable when studying finger tapping in subjects with disease or medication affecting heart rate. Also, the identification of coupling during the repetitive activity of small upper-extremity muscles suggests that neither increases in cardiac load nor impact-loading, two suggested explanations for why coupling occurs, are necessary for the phenomenon. Our findings are more consistent with the theories that optimization of blood flow to exercising muscles or neural interactions account for coupling.

P73.

The Application of Intersegmental Dynamics as a Means of Documenting Coordination Disabilities

T.B. HOSHIZAKI, V. VARDAXIS, K. MANAL and V. HATZITAKIS (Montreal, Quebec)

The effectiveness of medical treatments for improving movement deficiencies or assessing the effects of drugs on coordination is closely related to the ability of the practitioner or scientist to accurately and objectively evaluate the effect of their treatments. Much of the present research has consisted of simple movements involving single joint actions or simple tasks (Berardelli et al., 1986; Rogers & Chan, 1988; Montgomery & Nuessen, 1990). There is a clear need for valid and reliable test or tests to be developed that will document the characteristics of complex movement patterns. Research involving the interpretation of both kinematic and dynamic characteristics of movement patterns has established the importance of identifying functional phases in understanding movement organization (Feldman, 1980; Hoshizaki & Vardaxis, 1988). The purpose of this paper was to investigate the effectiveness of the Homogeneous Elements model in identifying subtle functional characteristics of a multi-segmental upper limb task. Four subjects were required to perform two tasks, one a sequential action involving extension at the elbow followed by horizontal abduction at the shoulder. The second task consisted of the two actions performed simultaneously. All actions were restricted to the horizontal plane. Distinct temporal and dynamic characteristics were identified for each task. The simultaneous task revealed two functional phases, 1. energy generation and transfer to the forearm (65%) and 2. energy absorption and transfer to the upper arm (35%). The sequence task revealed four functional elements, 1. energy generation (42%), 2. energy absorption and transfer to the upper arm (12%), 3. energy generation and transfer to the lower arm (33%) and 4. energy absorption and transfer to the upper arm (9%). The dynamic characteristics of each phase were also described using dynamic parameters; peak moment, peak power and peak acceleration. The analysis revealed unique dynamic characteristics for the two almost identical movements. The application of the proposed analysis to multi-segmental tasks has proven to be extremely effective in identifying distinct objective and functional characteristics of two similar, complex motor tasks. The advantage of identifying the actual deficiency using objective and quantitative parameters provide the practitioner and scientist with a powerful tool for assessing motor control treatments and the effect of drugs on coordination.

P74.

Chronic Intrathecal Baclofen for Intractable Spasticity by Daily Bolus Injections

H. HUGENHOLTZ, R.F. NELSON, E. DEHOUX and R. BICKERTON (Ottawa, Ontario)

Following completion of a double-blind crossover protocol of lumbar intrathecal bolus injections of baclofen solution and placebo saline into catheter access ports (CAPs) that culminated with 1 month of daily self-administered bolus injections of baclofen solution at a fixed dose, 6 subjects continued daily bolus injections of baclofen with dose escalations as required in order to optimize their spasmolysis for 5.5 - 12 months. Five of 6 subjects who were tested after 6 months of uninterrupted daily bolus injections maintained significant clinical improvement of the spasms, muscle tone and hyperreflexia in their lower limbs. Apart from one subject who attempted suicide with an overdose, there were no significant complications from chronic self-administered daily bolus injections of baclofen solution into CAPs. Chronic bolus injections of baclofen solution may provide an inexpensive treatment option for the management of patients with intractable spinal spasticity in selected circumstances.

P75.

Intrathecal Baclofen for Intractable Spinal Spasticity - A Double-Blind Crossover Comparison with Placebo in 6 Patients

H. HUGENHOLTZ, R.F. NELSON, E. DEHOUX and R. BICKERTON (Ottawa, Ontario)

Six subjects with intractable spinal spasticity completed a double-blind crossover paradigm in which they received intrathecal bolus injections of baclofen solution or placebo saline via an implanted catheter access port. Subjects were repeatedly tested with a multidisciplinary battery of clinical and physiological tests as well as a rating of quality of life. In contrast to the placebo saline, all subjects responded to the baclofen injections with clinically significant improvement in their lower limb spasms, muscle tone and hyperreflexia. The improvements were maintained following one month of daily self-administered intrathecal bolus injections at a fixed dose and resulted in improved quality of life.

P76.

Spasticity Assessment of Spinal Cord Injured Patients

P.W. NANCE and F. HU (Winnipeg, Manitoba)

Although spasticity is defined as hyperreflexia and a velocity dependent increased muscular tone, it is the latter which is the most

problematic to spinal cord injured (SCI) patients. Thirty-two SCI patients were assessed by measurement of 1) reflex activity, the Achilles Tendon Reflex (ATR), Soleus H-reflex, and the vibratory inhibition index of the H-reflex (VII) (100% relates to no inhibition), and 2) muscle tone using the Ashworth Score (AS) (1 = normal tone, 2 = a "catch", 3 = more than a "catch", 4 = passive movement difficult, 5 = limb is rigid). In 10 patients, the AS was compared to a modified Pendulum test. SCI patients with functional motor control of the legs demonstrated the greatest amplitude of ATR and H-reflex, and the lowest VII, relative to the other SCI patients. The AS did not differ among the patient groups. The pendulum score (5 minus the number of lower leg swings > 40 degrees in 3 sec.) correlated well with the AS, r = .93. These data suggest that the presence of problematic involuntary muscular dystonia is **not** correlated with hyperreflexia; in fact, only motor spared SCI patients demonstrate significant hyperreflexia. The VII failed to correlate with the ATR, R-reflex or AS. Although lacking a specific neurophysiological mechanism, the AS is a good clinical measure of problematic limb hypertonia. However, the pendulum test is also a good measure of subjective observation component which is the main limitation of the AS.

PWN is a Will-To-Win Scholar (Manitoba Paraplegia Foundation)

P77.

Biofeedback Rehabilitation is Effective in Chronic Facial Paralysis

I. DANYS, B. SEGAL, C. MELMED, M. BLACK, B. ARTHURS, M. SHAPIRO and I. ZOMPA (Laval; Montreal, Quebec)

When severe, unilateral facial paralysis persists more than two years following onset, no further spontaneous recovery is expected. We evaluated biofeedback rehabilitation in eleven such patients (2-12 years post onset of facial paralysis). The causes of facial paralysis were Bell's Palsy, acoustic neuroma, trauma and parotid tumour. All patients had intact, though abnormal, facial innervation as demonstrated by baseline electromyography and nerve conduction studies. At baseline, all patients had severe facial paralysis with House scores 3 to 5. Neuromuscular retraining was employed using a method similar to Balliet, Shinn, Bach-y-Rita (int. Rehab. Med. (1982) 4:67-74). To date, seven patients have completed six months of therapy and have undergone follow-up studies. Six of the seven patients have demonstrated significant improvement in facial paralysis, typically improving by one House grade. These results strongly suggest that effective facial rehabilitation is possible even after spontaneous recovery would no longer be expected.

I. Cerebrovascular

P78.

High Dose Thiopental Anesthesia for Open-Heart Surgery: A Retrospective Analysis of Neurologic Complications

B.A. ANDERSON, E.A. PASCOE, R.J. HUDSON, I.R. THOMSON, D.A. KASSUM, A. SHANKS and M. ROSENBLOOM (Winnipeg, Manitoba)

Neurological injury is a major complication of cardiopulmonary bypass (CPB). A single prospective study has shown that high-dose thiopental (HiTP) anaesthesia reduces the incidence of neurologic deficits in patients undergoing open-ventricle procedures. The use of HiTP is a controversial issue. Accordingly we reviewed our experience with HiTP over a 33-month period.

METHODS: HiTP was defined as a total dose greater than 15 mg/kg, titrated to produce burst suppression on the electroencephalogram. 240 patients undergoing surgery with opening of a left-sided chamber were reviewed. Data tabulated included cardiac index (CI) prior to CPB, operation performed, duration of CPB, type of oxygenator, need for inotropic support, the time to extubation, neurologic complications and survival.

RESULTS: There were 6 intraoperative deaths, none in HiTP group. Data from the 234 operative survivors are reported. 84 patients received HiTP; 150 patients received other anaesthetics (control). No differences were observed between groups with regard to operative procedure, duration of CPB, type of oxygenator, or lowest nasopharyngeal temperature. There were 5 intraoperative strokes (all control group). There were 9 perioperative strokes (2HiTP and 7 control).

DISCUSSION: Overall mortality was lower in the HiTP group. The incidence of intraoperative stroke was lower in the HiTP group, although this difference was not statistically significant. These data neither conclusively support nor contradict the use of HiTP to reduce neurologic injury during open ventricle cardiac surgery. Additional prospective trials are required.

P79.

Successful Thrombolysis of an Acute Basilar Occlusion Using Tissue Plasminogen Activator

P.A.B. BAILEY and M.H. BARRY (Saint John, New Brunswick)

While ongoing studies evaluate the use of Tissue Plasminogen Activator (TPA) in thrombotic stroke, anecdotal evidence of its effectiveness continues to accumulate. In the interim clinicians are left with difficult decisions in life threatening thrombotic stroke presentations, particularly in those involving the posterior circulation.

We report the successful lysis of an acute basilar occlusion using TPA. A 38-year-old male developed vertigo, dysarthria and headache during exercise. He presented in an ambulatory condition but suddenly deteriorated in a "locked-in" state. Immediate CT scan was negative. Angiography disclosed a low basilar occlusion. Three hours post occlusion, 100 units of TPA were administered over 90 minutes. Repeat angiography revealed the clot had lysed to a level distal to the superior cerebellar arteries. Clinical improvement occurred during infusion and continued for several hours. Minor left cerebellar dysfunction was the remaining deficit. Heparinization and subsequent long term anticoagulants were administered. No explanation for the thrombosis was uncovered despite appropriate investigation.

It is concluded that immediate administration of TPA in acute basilar occlusion is effective and that the benefits outweigh the risks.

P80.

Horner's Syndrome Secondary To Angiogram Negative, Extracranial Carotid Artery Dissection

M. ASSAF, P.J. SWEENEY, G. KOSMORSKY, A. WILBOURN and T. MAZARYK (Cleveland, U.S.A.)

A 59-year-old man presented with an acute Horner's Syndrome and symptoms suggestive of an ipsilateral carotid artery dissection. Carotid angiography was, however, normal. MRI imaging of the

neck and carotid arteries revealed a subadventitial carotid dissection explaining his symptoms, the Horner's and the normal angiogram.

Carotid artery dissection (CAD), previously considered rare, is increasingly reported because of better symptom and neuro-imaging recognition. CAD most commonly affects the extracranial carotid segment and is generally divided into two etiological categories: post-traumatic and spontaneous. With spontaneous dissection the underlying pathology can include fibromuscular dysplasia Marfanoid arteriopathy or primary intramural hematoma. Presumably an intimal tear, near the proximal end of the dissection, allows blood to track from the lumen into the arterial wall. In the common subintimal variety dissection of blood occurs beneath the intima, compromises the lumen and produces a characteristic angiographic picture. With the rarer subadventitial variety blood tracks outward, beneath the adventitia, sparing the lumen and sometimes producing a false aneurysm on the carotid wall. This may interrupt the sympathetic plexus and produce a Horner's Syndrome.

MRI may provide a non-invasive and reliable method of visualizing and following patients with subadventitial CAD.

P81.

A Comparison of Drawing Impairment Following Cortical and Subcortical Strokes

A. KIRK and A. KERTESZ (London, Ontario)

Constructional impairment is often considered a sign of cortical damage. Recently, aphasia, agraphia, and apraxia, disorders traditionally deemed cortical, have been well-described following focal subcortical lesions, suggesting an important role for subcortical structures in cognition. Constructional impairment following discrete subcortical lesions has not been systematically compared with that following cortical damage. We examined the relative incidence and severity of constructional impairment after cortical and subcortical strokes and whether there were qualitative differences between the drawings of these two groups. Spontaneous drawings of 125 patients with single hemispheric strokes (42 left cortical, 36 left subcortical, 20 right cortical, 27 right subcortical) were compared using a standardized scoring system previously applied in a variety of neurologic conditions. There was no significant difference in lesion volume between the four groups. Although previously noted right/left differences were confirmed, subcortical patients' drawings were indistinguishable on most measures from those of cortical patients. These data demonstrate that constructional impairment often follows subcortical strokes and is by no means an indicator of cortical lesion localization.

P82.

Hemispatial Neglect and Visual Search in Acute Stroke

S.E. BLACK and D.K. MARTIN (Toronto, Ontario)

To eludicate the spatial attention deficits underlying hemispatial neglect, we compared a standardized measure of neglect with performance on a visual search task in 66 (28 L, 38 R) patients consecutively admitted with a CT-verified, unilateral stroke, who were cooperative to testing within 60 days of onset. A weighted neglect score was derived from line bisection, drawings, line and figure cancellation tasks. Accuracy and speed of detection in left and right hemispace in a display of 86 drawings of familiar objects on a 20"x22" board (Kimura, 1986) was standardized in 26 age-matched controls. Subjects searched for a target which matched a stimulus placed in the centre of the board. Ten target items were bilateral, and 5 were present in each hemispace. Control subjects showed no side differences in search time; an assymmetry of 8.4 seconds was outside normal limits and defined as neglect. Patients without neglect had slower contralateral search time ($p < .001$), whereas those with neglect were slower in both hemispaces, though much more so contralaterally ($p < .005$). Neglect score and contralateral search time were significantly correlated ($p < .005$). 38 out of 66 subjects (11/28 L and 27/38 R) showed neglect on visual search compared to 33 of 66 subjects (6 left, 27 right), who showed neglect on the bedside battery. 28 of 38 subjects with visual search neglect had neglect on the battery; 28 of 36 subjects with bedside neglect also showed a neglect on visual search. We conclude that a contralateral impairment in visual search is found in focal brain damage, the degree of which is highly correlated with neglect. The visual search task can be administered at the bedside and is understood even by aphasic subjects. It is a sensitive, useful additional tool in the quantification of the neglect syndrome.

P83.

Glibenclamide Inhibits the Contractions Induced by Prostaglandin $F_{2\alpha}$ and Oxyhemoglobin in Canine Middle Cerebral Arteries In Vitro

H. ZHANG, B.K.A. WEIR, N. STOCKBRIDGE and D. COOK (Edmonton, Alberta)

Glibenclamide, a sulfonylurea which is used for the treatment of non-insulin dependent diabetes mellitus, was employed as an antagonist to inhibit the contractile responses of canine middle cerebral arteries to KCl, NA, 5-HT, prostaglandin $F_{2\alpha}$ and oxyhemoglobin. Isometric contractions were recorded in 4 rings for each agent and compared using analysis of variance. We found that 1) glibenclamide (1 and 10 μM) had no effects on the contractions induced by KCl, NA and 5-HT; 2) glibenclamide (1 and 10 μM) inhibited the contractile responses of canine middle cerebral artery rings to prostaglandin $F_{2\alpha}$; 3) glibenclamide (10 μM) partly inhibited the contractile responses of canine middle cerebral artery rings to oxyhemoglobin (10 μM); 4) glibenclamide (5-10 μM) fully relaxed the precontractions by prostaglandin $F_{2\alpha}$ (3 μM) and oxyhemoglobin (10 μM). Previous reports note the inability of glibenclamide to inhibit contractions of peripheral arteries by KCl, NA, angiotensin II, caffeine and endothelin 1. We concluded that since glibenclamide selectively inhibits the contractions of canine middle cerebral arteries to prostaglandin $F_{2\alpha}$ and oxyhemoglobin, the spasmogenic effects of oxyhemoglobin may be partly mediated by the release of prostaglandins. Since prostaglandins play an important role in the regulation of cerebral vasculature, the possible usage of glibenclamide in the treatment of cerebral disorders, especially cerebral vasospasm after subarachnoid hemorrhage, deserves further study.

P84.

Lipid Profile of Stroke Patients: A Prospective Study in 59 Patients and 60 Age Matched Controls

A. SHUAIB, J. KALRA, M. PRASAD and S.V. MANTHA (Saskatoon, Saskatchewan)

The dramatic decline in stroke during the last 5 decades is likely due to control of risk factors, especially hypertension. An increase in LDL cholesterol (chol) or a decrease in HDL chol may be addi-

tional risk factors for cerebrovascular disease. In this study we prospectively evaluated patients with ischemic stoke (except cardioembolic) and age matched controls for serum chol, triglycerides (trig), LDL and HDL chol, and apolipoprotein (apo) A&B levels. None of the patients had a history of cardiac disease (myocardial ischemia has been shown to increase serum apo B levels). Between Sept. 1989 and Sept. 1990, 59 patients (m = 43, f = 16 age = 65) and 60 controls (m = 23, f = 37 age 67) were investigated. No differences were found between the total chol, trig, LDL chol, apo A&B between the two groups. HDL chol, trig, LDL chol, apo A&B between the two groups. HDL chol was found to be significantly lower in the stroke patient ($p < 0.05$). In stroke patients, total chol ($p < 0.05$), LDL chol ($p < 00.05$) and apo B ($p < 0.05$) was significantly higher in female patients.

This study confirms that low HDL chol may be a risk factor for stroke. Additionally, we show that lipid abnormalities appear to be more severe in women.

P85.

Risk Factors for Ischemic Stroke: A Population Based Study

L. LUI, A. SHUAIB and B. REEDER (Saskatoon, Saskatchewan)

It is widely believed that the dramatic decline in the incidence of stroke over the last 6 decades is a result of better control of stroke risk factors. Most of the epidemiological work on risk factors for stroke has come from the Framingham population. This present report is based on a population study of 2,168 subjects in Saskatchewan, in whom a detailed history for atherosclerosis and lipid data were obtained. There were forty-one patients (male = 21, female = 20), who had suffered an ischemic stroke. The following "stroke risk factors" were found to be significant when these patients were compared to the remaining study population: Hypertension ($p < .05$), previous myocardial infarction ($p < .05$), family history of stroke ($p < .05$) and diabetes ($p < .05$). Lipid abnormalities and smoking were not significantly different in the two groups.

While confirming that hypertension, heart disease and a family history are risk factors for stroke, our study also reveals that lipid abnormalities and smoking were not significantly different in the two populations in Saskatchewan, Canada.

P86.

Decrease in Partial Thromboplastin Time and Prothrombin Time in Acute Thrombotic Stroke

S.R. LAM, A. SHUAIB and S. RUTLEDGE (Saskatoon, Saskatchewan)

There is anecdotal evidence to suggest that the partial thromboplastin time (PTT) is often shortened in patients with acute stroke. It has been suggested that the prothrombin time (PT) may also be reduced. However, there have been few studies to substantiate this. A reduction in the PTT and PT may be indicative of a pro-coagulant state.

The charts of patients with a discharge diagnosis of acute stroke were reviewed. Forty-three patients were identified who had sustained a stroke not attributable to haemorrhage or cardiac embolus. In all these cases the PTT and PT had been measured during the acute period. The results were compared with an age-matched control group of patients in whom the PTT and PT had been determined prior to elective cardiac catheterization.

The mean PTT ratio (patient PTT: laboratory control PTT) in the stroke patients was 0.945 compared to 1.02 in controls ($p < 0.05$). The mean PTT difference (patient PTT minus control PTT) was -1.72 second (s) in stroke patients compared to +0.632s in the controls ($p < 0.05$). Similarly, the mean PT ratio was 0.951 in stroke patients compared to 1.03 in controls ($p < 0.001$) and the mean PT difference was -0.581s in stroke patients compared to +0.263s in controls ($p < 0.001$).

Our results suggest that there may be a thrombotic predisposition in patients with acute stroke. If this is confirmed, therapeutic measures directed at reversing this pro-coagulant state may be indicated. However, it is also possible that the results may represent a physiological response to acute injury. To further evaluate these possibilities, studies are underway to determine if these findings are also present in patients with strokes due to other aetiologies.

J. Movement Disorders

P87.

Striatonigral Degeneration: Two Patients with Clinical, MRI, Histochemical and Pathological Correlation

T.G. CURRAN, J. PROVIAS, C. BERGERON and A.E. LANG (Toronto, Ontario)

Despite several studies correlating poor levodopa responsiveness and abnormal hypointense signals in the basal ganglia on heavily weighted T2 images (believed to represent, at least in part, deposition of iron) there has been only one reported case with MRI-pathological correlation. We report two additional cases of pathologically proven striatonigral degeneration (SND). Both had parkinsonism with minimal or unsustained benefit from levodopa. The MRI findings in both revealed markedly atrophic putamen and on heavily weighted T2 images there were prominent hypointense signals in the striatum especially the putamen producing a "slit-like void signal". Both patients were diagnosed as having SND in life with clinical features and MRI. Postmortem in both confirmed the classical pathological features of SND (one pure-SND and the other more diffuse multiple system atrophy (MSA) with maximum severity in the dorsolateral putamen). Histochemical analysis confirmed the presence of large amounts of iron in the putamen and at the cellular level a significant amount of the iron was found in neurons. Similar iron deposition is not seen in the striatal gliotic degeneration of Huntington's disease but this may be a reflection of severity. We conclude that SND has a typical MRI picture which helps to distinguish it from other causes of parkinsonism. Further MRI, pathological and histochemical correlative studies are needed to fully understand the significance of the MRI abnormalities in relation to iron and other magnetic compounds. The role of abnormal iron deposition in the striatum of SND may play an important role in the pathogenesis, possibly through facilitation of oxidative reactions which generate cytotoxic free radicals. Assessment of MRI changes may also be important in determining the effects of therapy directed at altering the natural course of SND and other MSAs.

P88.

Atypical Clinical Features and Normal Autopsy in Therapeutic Trials in Parkinson's Disease

D.A. GRIMES, J.D. GRIMES, P.A. GRAY, E. MOHR and B. LACH (Ottawa, Ontario)

There is interest in treating mildly affected Parkinson's disease (PD) patients with agents which may delay disease progression.

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Patients with essential tremor may present diagnostic difficulty. Two patients, diagnosed as PD and treated and followed in therapeutic trials are reviewed. At autopsy no significant neuropathological abnormality was found in either patient. One patient had moderate rest and minimal postural and action tremor of recent onset (4 months). He also had minimal rigidity and bradykinesia. He was treated with deprenyl and died of ischemic heart disease 19 months later. The second patient presented with minimal rest tremor and more prominent postural and action tremor. During her 10-year clinical course she responded to, and was worse off, antiparkinsonian drugs including Pergolide. She developed end of dose failure, dystonia and blepharospasm. She had a bradykinetic gait with functional features. Both patients had increased rest tremor when walking.

Even with the most careful clinical exam and adherence to accented diagnostic features, mistakes may be made. The clinical diagnosis of PD can be inaccurate because of atypical features of essential tremor with the recent onset of rest more than postural or action tremor; placebo response to antiparkinsonian drugs; and functional features on clinical exam. In organizing and interpreting therapeutic trials one must consider these types of patients in addition to those with Parkinson-plus syndromes.

P89.

Pulmonary Embolism: An Underrecognised Yet Frequent Cause of Death in Patients with Parkinson Syndrome

R. MOSEWICH, A.H. RAJPUT, B. ROZDILSKY and A. SHUAIB (Saskatoon, Saskatchewan)

Previous reports on the cause of death in patients with Parkinson syndrome (PS) have lacked post mortem verification in most cases. These reports do not find that pulmonary embolism (PE) is a frequent cause of mortality in these patients. In our institution, between 1969 and 1989, 235 patients with PS died. Of these, 60 complete autopsies were performed. 26 patients had pure Lewy body disease and 34 patients had other causes of PS or Lewy body disease in addition to other degenerative cerebral pathology. The causes of death in all patients combined were: pneumonia 34(56.7%), PE 8(13.3%), myocardial infarction (MI) 6(7.5%), pulmonary edema 4(6.8%), stroke 2(3.3%) and unknown 9(15%). In patients with pure Lewy body disease, the causes of death were pneumonia 14(53.8%), PE 6(23.1%), MI1(3.8%), stroke 1(3.8%), pulmonary edema 3(11.5%) and unknown 3(11.5%). In patients with other causes of parkinsonism the causes of death were pneumonia 20(58.5%) MI 6(17.6%), PE 2(5.9%), stroke 1(2.9%) and unknown 6(17.6%).

Our results indicate that in addition to pneumonia and cardiovascular disease, PE is a common cause of mortality in patients with PS. Furthermore, PE occurs significantly more frequently in the pure Lewy body disease group.

P90.

Movement Disorders in Aids

A. DUROCHER and P. DUQUETTE (Montreal, Quebec)

Movement disorders in AIDS are a relatively infrequent presentation; in particular, there have been so far few reported cases of ballism. We describe the case of a forty-five-year-old patient with presumed cerebral toxoplasmosis showing severe hemi-ballism; a video document accompanies the presentation.

Treatment given is discussed with reference to the pertaining literature; extra-pyramidal disorders encountered in AIDS are also reviewed. It is suggested that as prevalence grows and more cases are encountered, a quick and systematic approach to these problems will be needed.

K. Neuromuscular

P91.

Co-occurrence of Juvenile Amyotrophic Lateral Sclerosis and Multiple Sclerosis: A Case Report

M.J. STRONG, A.J. HUDSON and W.F. BROWN (London, Ontario)

We report the exceptional case of a 38-year-old caucasian female who, at the age of 18 years, insidiously developed a flaccid/spastic dysarthria with tongue wasting and fasciculations, prominent upper extremity wasting with weakness and fasciculations, and diffuse spasticity–most prominent in the lower extremities. Repeated EMG studies during the next 20 years confirmed active denervation in all extremities, hypercomplex motor unit potentials and significant reductions in motor unit estimates. Transcranial cortical stimulus evoked motor responses were absent. Percutaneous quadriceps muscle biopsy showed neurogenic atrophy without evidence of a primary muscle or mitochondrial disorder. Diaphragmatic involvement was present (maximum phonation time of 8 seconds with formed vital capacity and mean inspiratory and expiratory pressures reduced to 55, 48 and 37% of predicted values, respectively).

At the age of 38, the patient experienced a single episode of sudden right hemiparesis sparing the face accompanied by right knee numbness and a complete loss of vision in the right eye. Reviewed 5 months later, all symptoms had resolved, but right temporal pallor was present. MRI demonstrated discrete regions of increased signal intensity compatible with demyelination in multiple periventricular and deep white matter regions. The visual evoked potentials was markedly delayed on the right (208 msec). Oligoclonal banding was present.

Amyotrophy has been well described in long-standing MS, as have been fibrillation potentials in the acute encephalomyelopathic form. A single adult onset case of ALS has been described in a case of chronic relapsing/remitting MS. Based on the combined clinical electrophysiological and histological evidence, we believe this to be an example of juvenile ALS with long-term survival and the subsequent development of MS. Although the probability of such a co-occurrence is approximately 1×10^8, and likely related to chance alone, the possibility of an underlying genetic predisposition common to both disorders cannot be ignored.

P92.

Excitatory Amino Acid Receptor Antagonists in Murine Motoneuron Disease

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Excitatory neurotoxic agents have been suggested as possible causes for amyotrophic lateral sclerosis (ALS).

We have examined the ability of antagonists of excitatory amino acid (EAA) receptors to halt or retard the progression of neurological symptoms in a murine model of ALS.

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The wobbler mouse (wr/wr) is an autosomal recessive mutant in inbred CS7BL/Fa mice which develops degeneration of motoneurons within the brainstem and spinal cord. By 3-4 weeks of age, wobbler mice gain weight less than normal littermates and develop progressive neurological symptoms including tremor, a gait disorder, forepaw weakness and atrophy, as well as extraocular muscle involvement. Treatment of wobbler mice with daily subcutaneous injections of N-methyl-D-aspartate (NMDA) receptor antagonist (+)-5-methyl-10,11-dihydro-5H-dibenzo(a,d) cycloheptan-5, 10-imine maleate (MK-801) in doses of 0.25 (n = 6) and 0.5mg/kg (n = 2) did not retard neurological deterioration as assessed by a semiquantitative clinical scale compared to saline treated wobbler mice (n = 5). Injections were begun within 4 days of birth and continued for 12-13 weeks.

We conclude that NMDA receptor activation is probably not involved in the pathogenesis of murine motoneuron disease.

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P93.

Mitochondrial Myopathy with Progressive External Ophthalmoplegia in a Child

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The clinical onset of mitochondrial myopathy characterized by progressive external ophthalmoplegia (PEO) is generally in childhood, although the etiology is usually established in adult life (Holt, et al 1989). We, therefore, report the clinical, electron microscopic and mitochondrial genome studies in an 8 year old.

This boy was seen at the age of 7 years with a 3 year history of ptosis and PEO. In addition to these findings, he also had bilateral weakness of facial, sternomastoid and limb (power: 3+ upper and 4+ lower, proximal weaker than distal) muscles. Normal investigations included CT and MRI scans of the brain, serial nerve conduction studies, repetitive stimulation, SEP, BAEP, ERG, cardiac assessment, urine and plasma aminoacids, urine organic acids and capillary lactates. The CSF protein was elevated on 2 occasions (0.98 g/L and 1.23 g/L; normal 0.2-0.4 g/l); CSF lactate was in the high normal range (2.1 mmol/L and 2 mmol/L; normal 0.5-2.2 mmol/L). EMGy showed a myopathy. Ragged-red fibres containing many pleomorphic mitochondria were found in biopsies of sternomastoid and quadriceps muscles; mitochondrial inclusions were not seen. Many fibres failed to stain for cytochrome oxidase (complex IV). Southern blot analysis on DNA (sternomastoid muscle) showed a large deletion of about 8-9 Kb in 76% of total muscle mitochondrial gnomes. The deletion affected subunits of all respiratory chain complexes as well as several genes coding for tRNAs. He is being treated with Coenzyme Q.

Such cases can now be diagnosed earlier in life but can long term outcome be improved by early recognition?

P94.

Palmar Itching with Carpal Tunnel Syndrome

A.J. WILBOURN and P.J. SWEENEY (Cleveland, U.S.A.)

Patients with carpal tunnel syndrome (CTS) experience several different upper extremity sensory phenomena, including: painless "pine/needles" finger paresthesia; spontaneous Tinel's sign on wrist flexion; hand/finger "swelling" or "thickness" sensations; painful prickly finger paresthesia; absence of sensation in the median fingers; deep volar forearm arching. The last three occur with more severe CTS, as determined by median nerve conduction studies (NCS). One CTS-induced dysesthesia, virtually unmentioned in Neurology and Dermatology texts, is palmar and median-innervated finger itching. Of 50 patients with NCS-proven CTS surveyed, 9 had such symptoms, affecting the palm alone, or the palm plus one or more median-supplied fingers; these were often associated with "pins/needles" paresthesia, but sometimes occurred alone. Although typically short-lived and mild in degree, itching in three patients was intense, persistent, and the dominant CTS symptom (the only symptom in one). Several patients were thought to have detergent allergies; two had been referred to dermatologists.

Conclusion: CTS can cause palmar/median finger itching. Failure to appreciate this uncommon presentation can delay diagnosis and appropriate treatment.

P95.

Neurogenic Muscle Hypertrophy of the Upper Extremity

P.R. BOURQUE and D.N. PRESTON (Ottawa, Ontario)

Neurogenic muscle hypertrophy was first described by Jean L'Hermitte in a patient with thenar/hypothenar hypertrophy consecutive to a forearm injury. Later reports have focused mainly on hypertrophy of the calf in patients with S1 radiculopathy, spinal muscular atrophy, HMSN 1 and 2 or after polio-myelitis. We describe 2 patients with focal proximal neurogenic muscle hypertrophy of the upper limb.

A 42-year-old man, 6 years after otherwise typical idiopathic brachial neuropathy, was found to have hypertrophy of the right trapezius muscle. This muscle was now of normal strength and normal by EMG, although mild paresis and acute denervative changes had been documented 6 years previously. CT scan of the trapezii showed symmetrical muscle attenuation coefficients, and confirmed the relative hypertrophy on the right side.

The second case, a 54-year-old man, had presented with bilateral brachial plexus neuropathies and was followed over a 7 year period. The right deltoid muscle was initially severely weak and showed marked EMG abnormalities consistent with denervation. Six years later striking hypertrophy had developed although needle EMG still showed marked abnormal spontaneous activity (fibrillations, positive sharp waves) and decreased recruitment. Polyphasic motor unit potentials of long duration were noted.

Focal muscle hypertrophy can occur several years following brachial neuropathy with partial denervation. Two different patterns are presented:

a) full recovery of strength, normal EMG
b) severe residual paresis and EMG evidence of ongoing denervation/reinnervation

P96.

Modified Quantitative Sweat Axon Reflex Testing (QSART) in Diabetic Neuropathy

J.D. STEWART, D. NGUYEN and M. ABRAHAMOWICZ (Montreal, Quebec)

Question: In diabetic peripheral neuropathy, how frequently are small diameter nerve fibres involved?

Methods: The capsule designed by Low was used to ion-

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tophorese acetylcholine into the skin on the foot and wrist. This stimulated sweat glands **directly** and other sweat glands **indirectly,** the latter via an axon reflex. Sweat droplets were recorded using a silastic patch and counted using computerized scanning. Responses from normal volunteers were compared with those of patients with diabetic neuropathy.

Results: Of the direct and indirect responses in hand and foot, the indirect responses from the foot were significantly different: Normal volunteers mean numbers of sweat droplets 155 ± 55; diabetic patients 45 ± 52.

Conclusions: In a high proportion of patients with diabetic neuropathy there is involvement of small diameter peripheral nerves. The indirect response of the modified QSART in the foot is an effective method for assessing these as represented by the sympathetic sudomotor fibres.

1. Low PA, Caskey PE, Tuck RR, et al. Quantitative sudomotor axon reflex test in normal and neuropathic subjects. Ann Neurol 1983; 14: 573-580.
2. Kennedy WR, Sakuta M, Sutherland D, et al. Quantification of the sweating deficiency in diabetes mellitus. Ann Neurol 1984; 15: 482-488.

P97.

Sympathetic Skin Response (SSR) Testing: What's Normal?

D. LAMOUREUX, J.D. STEWART, L. TOMBARI and S. MURRAY (Montreal, Quebec)

SSRs are of value in assessing unmyelinated nerve fibre function in peripheral neuropathies. The easiest method to stimulate the patient is an electric shock to a peripheral nerve.

Questions: How many stimuli are required to evoke SSRs in normal persons? Do auditory stimuli work as effectively?

Methods: Thirty-one healthy volunteers age 20-70 had a brief questionnaire, examination, and nerve conductions to conform the absence of peripheral neuropathy. SSRs were tested by stimulating the median nerve 10 times at intervals >15 seconds and recording from the palm and sole. If less than 2 responses occurred in the palm or sole, an auditory stimulus was used. In the second phase of the study, 8 of the volunteers were tested with an auditory stimulus.

Results: 30/31 subjects had 2 or more responses to electric shocks. The one non-responder also did not respond to 10 auditory stimuli. Eight volunteers who responded normally to electric shocks were subsequently tested with auditory stimuli; all had fewer responses, 2 volunteers having less than 2 responses.

Conclusions: If a patient has less than 2 SSRs to 10 electric shocks, it is highly probable that he/she is abnormal. Auditory stimuli are inferior to electric shocks in evoking SSRs.

P98.

Surgical Techniques for Recovery of Elbow Flexion Following Brachial Plexus Injury

M. PREUL and P.M. RICHARDSON (Montreal, Quebec)

Injured nerves to proximal muscles of the arm or corresponding elements of the brachial plexus can often be satisfactorily repaired by direct suture or use of a nerve graft. Other techniques are required when the corresponding spinal roots have been avulsed or severely injured. Because of some dissatisfaction with the results of intercostal-to-musculocutaneous nerve grafts, two other sources of neurotisation were tried. In two patients with lesions of the upper trunk or roots, a functional thoracodorsal nerve (nerve to latissimus dorsi) was sacrificed and directly joined to the musculocutaneous nerve. Good elbow flexion (grade 4/5) was obtained with acceptable loss of shoulder function. In a single patient with virtually no function of the brachial plexus the spinal accessory nerve was sacrificed distal to most of its branches and joined by sural nerve graft to the musculocutaneous nerve. This previously described procedure yielded satisfactory elbow flexion (grade 3/5) without significant loss of trapezius or sternomastoid function. In appropriate circumstances, either of these methods can help to reinnervate the biceps muscle after brachial plexus injury.

P99.

Severe Phenytoin Hypersensitivity with Myopathy; A Case Report

C.A. BARCLAY, M. MCLEAN, H. HAGEN, A.K.W. BROWNELL and M.E. MACRAE (Calgary, Alberta)

Since its introduction, more than 50 years ago, phenytoin has been found to be a remarkably safe anticonvulsant. Significant side effects, although rare, do occur. These include Stevens-Johnson syndrome, hepatic necrosis, polyarteritis nodosa, and serum sickness. Inflammatory myopathy, as a side effect, is extremely rare, with only four cases having been reported in the literature.

We report the case of a 45-year-old woman with a glioblastoma multiforme and seizures who developed a severe reaction to phenytoin. This consisted of toxic epidermal necrolysis, elevated liver enzymes, and a diffuse myopathy with prominent bulbar features. Laboratory abnormalities included a creatine kinase elevation of over 4,000, an EMG showing small polyphasic potentials and fibrillation potentials and an abnormal muscle biopsy. After discontinuation of her phenytoin and treatment with a shot course of steroids, her symptoms resolved within one month.

We conclude that myopathy, although rare, can be a feature of phenytoin hypersensitivity.

L. Neurophysiology

P100.

Unusual Absence of Spontaeous Activity on Needle EMG Study in Uremic Patients

S. BURTON, H. REMTULLA, C. BOLTON, O. MARYNIAK and J. BROWN (London, Ontario)

We present two patients who illustrate this unusual phenomenon.

A 68-year-old patient had progressive wasting and weakness of limb muscles for four months. He was a Type II diabetic who suffered from endstage renal disease and had been receiving chronic hemodialysis for one year. Nerve conduction studies pointed to a moderately severe motor and sensory polyneuropathy in which there had been primary axonal degeneration of nerve fibres. Needle EMG revealed an absence of abnormal spontaneous activity and relatively normal motor unit potentials on quantitative EMG. Muscle biopsy of upper and lower limbs showed mild to moderately severe denervation atrophy.

A 32-year-old man on long-term chronic hemodialysis had removal of a transplanted kidney that had been rejected. There was inadvertent trauma to the femoral nerve, which resulted in severe,

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and persisting, wasting and weakness of muscle. Three months later, with stimulation of the femoral nerve, the quadriceps compound muscle action potential could not be recorded. Needle electromyography revealed no abnormal spontaneous activity and decreased insertional activity. No motor unit potentials were recruited.

Our findings suggest either a severe metabolic disturbance of muscle fibre membranes, or a failure of expected denervation hypersensitivity to develop. The phenomenon is presumably unique for uremic patients who have muscle denervation.

P101.

Phrenic Nerve Conduction

F. GRAND'MAISON, C.F. BOLTON, A. PARKES and L. BERNARDI (Sherbrooke, Quebec; London, Ontario)

Despite descriptions of this technique by Newsome-Davis (1967) and Markand, et al (1984), it has been rarely used, perhaps due to concerns regarding technical accuracy. We have utilized the technique, paying particular attention to electrode placement and EDG artifact. The surface electrodes used to stimulate the phrenic nerve in the neck cause little discomfort. Stimuli were given during quiet respiration. Studies were performed on 9 healthy individuals, repeating the test twice in each, to determine repeatability. Comparisons were made to median nerve motor conduction studies, recording from the thenar muscle. Repeatability was expressed as a percentage value for the ratio of the difference of test one and test two over the mean, for the various compound action potential measurements, mean (range) %: amplitude - diaphragm 15 (4-29), thenar 17 (2-39); latency - diaphragm 6 (0-17), thenar 8 (3-11); duration - diaphragm 16 (2-25), thenar 30 (7-51). Thus, phrenic nerve conduction studies are just as accurate as standard motor conduction studies. They should be used routinely to investigate the many neuromuscular disorders that may affect respiration.

P102.

Preclinical Detection of Cervical Spondylotic Myelopathy (CSM) Using Transcranial Magnetic Stimulation

A. TRAVLOS, A. EISEN and B. PANT (Vancouver, British Columbia)

Cervical spondylotic myelopathy (CSM) is the most serious complication of cervical disc degeneration (CDD). It usually develops insidiously and once clinically evident surgical intervention can achieve little more than impede progression. We describe evidence for preclinical CSM, associated with CDD, which might allow for more timely surgery. Eighteen patients (mean age 48.8 years) with CDD were studied with transcranial magnetic stimulation. All had CT confirmed, unilateral C5 or C6 radiculopathy, without clinical or radiological evidence of CSM.

Motor evoked potentials (MEPs) were elicited from the thenar and/or hypothenar muscle complexes (C8/T1) ie, at least 2 segments caudal to the involved root. The group mean thenar compound muscle action potential (CMAP) amplitude was normal (14.1 ± 6.2mV) but in 10 patients (55.6%) the MEP amplitude was reduced (mean 4.5 ± 3.4mV). The MEP/CMAP ratio, which takes into consideration any peripheral muscle wasting, was also very reduced in the same patients (mean = 31.9 ± 7.8%). Normal, aged matched, values are: MEP amplitude >7.5mV and MEP/CMAP ratio >64% respectively. Central motor delay between the motor cortex and the lower cervical cord was prolonged in 4 of the patients whose MEPs were reduced in amplitude.

The findings suggest that "physiological" cord compression commonly complicates CDD without overt clinical or radiological CSM. Central motor pathway assessment can be used to follow its progression and may be a measure for more timely surgical intervention.

P103.

A Single Neurophysiological Test Used to Quantitate ALS Progression

A.A. WILFONG, J.M. KILLIAN and S.H. APPEL (Houston, U.S.A.)

Neurophysiological tests may be useful adjuncts in monitoring disease progression in amyotrophic lateral sclerosis (ALS) patients. Determination of the compound muscle action potential (CMAP) amplitude from the trapezius muscle is an easily performed and highly reproducible test which causes minimal discomfort. This test provides a quantitative index reflecting the number of remaining motor units supplied by the spinal accessory nerve. The trapezius muscle does not become clinically atrophic until very late in the course of ALS. Therefore, although of limited utility in the early phases, this test may be helpful throughout the majority of the disease course.

The amplitude of the trapezius CMAP was followed serially in 30 ALS patients. The amplitudes were correlated with scores from an extensively studied clinical rating scale. Twenty-four patients clearly demonstrated clinical deterioration based on the rating scheme. In 21 of these patients, a decrease in CMAP amplitude correlated with the deterioration in clinical status. No correlation was found in 3 of the 24 patients, 2 of whom showed no significant change in CMAP amplitude and 1 who showed an increase in amplitude. In 6 of the 30 patients, no clinical deterioration was noted. Four of these patients had CMAP amplitudes paralleling their clinical course and 2 had amplitudes which did not correlate with the rating scale.

In this series, the trapezius CMAP amplitude was predictive of the clinical status except in the earliest stages of the disease. In the majority of patients, serial follow-up demonstrated a correlation between the CMAP amplitude and the clinical status over time. Thus, this simple and reliable monitoring procedure may prove to be a useful tool in objectively following ALS patients enrolled in new therapeutic studies.

P104.

Rearrangement of Motor Units in Different Stages of Denervations-Reinervations Process — A Clinico-Electromyographic Study

O.W. FARRONAY, S.S. NIKITIN and L.F. KASATKINA (Moscow, USSR).

The comparison of EMG changes of motor unit potentials (MUP) duration and histochemical reorganization of MU was made at various stages of denervations-reinervations process (DRP) in 134 deltoid muscles in patients with different neuromuscular diseases: myasthenia (33), inflammatory myopathy (44), polyneuropathy (25), amyotrophic lateral sclerosis (32). The EMG stage of DRP was estimated according to the classification proposed by Gecht et al (1983). The cryostat sections of biopsy samples of the same muscles were stained to demonstrate the activity of mATPase at pH 9.4.

In each sample the random area of total 200 fibres was analysed and the number of grouped muscle fibres of the same type were calculated. Independently of nosological form at 1-2 EMG stage the number of grouped muscle fibres of I or II type was not more than 10 in 80% of muscles, at the stage 3 in 76% of muscles the number of grouped fibres was not less than 11-20 and at the 4-5 stage in 70% of muscles – not less than 21-30 fibres. The results indicate that the morphological rearrangement of muscle can be seen at the very early stage of DRP and even when there is no reinnervated MUPs of long duration. The changes of muscle fibre distribution at the 1-2 EMG stage confirmed by the increased fibre density (FD) studied by the SFEMG electrode correlation between the increased FD and MUPs with long duration (R = 0.4; p 0.05). There is a strong correlation between the MUPs with increased mean duration and the mean number of grouped muscle fibres in patients with neurogenic disorders (R = 0.5; p 0.01).

The results of this study can help to discuss the problem of compensatory innervation, patterns of its development in different neuromuscular diseases.

P105.

Somatosensory Evoked Potential Studies in Type I Diabetes Mellitus

H.Z. DARWISH, K. MORRISON and D. STEPHURE (Calgary, Alberta)

The exact pathogenesis of diabetic peripheral neuropathies remains unknown, and is suspected to result from the interaction of multiple factors. The recent demonstration of metabolic accumulation of sorbitol and reduction of nerve free myoinnositol in the peripheral nerve, has led to trials of therapy with aldose reductase inhibitors and dietary myoinnositol supplementation in patients with clinical neuropathy. Electrophysiologic studies in Juvenile diabeties have demonstrated abnormalities in distal sural and peroneal conduction in asymptomatic patients.

We have embarked on a program of testing distal and proximal motor nerve conduction (MNC) and somatosensory evoked potentials (SEP) to define the presence of "subclinical neuropathy" in asymptomatic children with a duration of juvenile diabetes mellitus (JDM) greater than 10 years. A group of 26 such children has been defined. To date we have completed testing in 13.

MNC studies in median, peroneal, and posterior tibial nerves, including F wave studies in peroneal and posterior tibial revealed a mild delay in 1/13.

Sensory nerve action potential studies, and SEPs to sural, posterior tibial and median nerves have demonstrated abnormalities in another 8/13. One child had a partial conduction block in the distal median nerve and one demonstrated delay in proximal conduction in sural and posterior tibial nerve. 4/8 had significant suppression or absence of the N28-P37-N45 SEP complex to posterior tibial nerve stimulation and 2/8 had absence of the SEP to sural nerve stimulation.

It is possible that specific intervention early and before clinical neuropathy is established may prevent debilitating and refractory neuropathy. Further long term studies will be necessary to prove that the SEP changes described are associated with later clinical neuropathy and that early intervention may reverse such changes.

P106.

Auditory Evoked Potentials Recorded Using Maximum Length Sequences

T.W. PICTON (Ottawa, Ontario)

Auditory evoked potentials were recorded in fifteen subjects using a maximum length sequence analysis. The number of elements in a maximum length sequence is one less than a power of two (i.e., 7, 15, 31, etc.). The sequence contains a particular mixture of stimuli and non-stimuli with the number of stimuli being one more than the non-stimuli. A minimum interval is chosen and the stimuli are presented (or not) at these intervals according to the sequence. The sequence is repeated many times and an average response is recorded to the entire sequence. A deconvolution procedure can then separate out the response to a single stimulus from the overlapping waveforms in the response to the sequence of stimuli. This technique recognizes evoked potentials at rates of stimulation that would cause a very confusing overlap of responses with simple averaging. Auditory brainstem responses can be recorded at stimulus rates of several hundred per second. The middle latency responses can be recorded at rates of stimulation of over 40/s and the late auditory evoked potentials at rates of over 2/s. This technique has clear clinical advantages when speed is essential. The technique may therefore become important in recording auditory evoked potentials to assess the hearing of children, or to monitor either the integrity of the auditory pathway of the state of anesthesia during an operation. The technique may also be helpful in studying neurological disorders that only affect the auditory system at rapid stimulus-rates.

P107.

Is Timing a Factor in Detecting Abnormalities on EEG in Lacunar Stroke?

T.E. HOGAN and A. SHUAIB (Saskatoon, Saskatchewan)

Cranial CT (CCT) scans are normal in most patients acutely after a lacunar stroke. We have previously shown that the combination of CCT, standard EEG and EEG mapping can detect abnormalities in 72% of patients following lacunar infarction. Also a combination of EEG and EEG mapping showed significantly more abnormalities than CCT. This study was undertaken to assess the time relationship between onset of lacunar stroke and time of testing to determine whether electrophysiological testing performed closer to the event is more likely to detect abnormalities. A total of 32 patients with acute lacunar infarction admitted to the Stroke Unit were prospectively evaluated. There were 10 patients tested with EEG and EEG mapping within three days and 22 patients beyond 3 days. Results showed for standard EEG, 9 of 22 patients (41%) had abnormalities beyond 3 days, 5 of 10 patients (50%) within 3 days. EEG mapping showed 10 of 22 patients (45%) had abnormalities beyond 3 days, 5 of 10 patients (50%) within 3 days.

Our study showed no significant increase in sensitivity when tests were performed within 3 days of event. We therefore believe that delaying the study until after the initial period following acute stroke, when patients may be unstable, will not influence outcome of test results.

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P108.

EEG and Clinical Neurological Predictors in the ICU

G.B. YOUNG, J. WEITENDORF and J. KREEFT (London, Ontario)

While intensive care units (ICUs) have utilized a severity of disease classification systems to help to prognostically stratify critically ill patients, neurological, especially neurophysiological, aspects have not been emphasized. We undertook this survey to determine the usefulness of the neurological examination and electroencephalograms (EEGs) in determining outcome in an unselected collection of comatose patients in a large tertiary general hospital ICU.

We evaluated 200 consecutive comatose patients who had EEGs in the ICU. The following were tabulated: age, sex, etiology of coma, EEG classification, EEG reactivity to stimuli and the outcome of each patient. We excluded children under 8 years of age, cases of drug intoxication and cases which met the clinical criteria for brain death.

The following variables showed a significant relationship to mortality: etiology of coma (higher with anoxic-ischemia than with septic/other metabolic causes), age (directly related to mortality), absence of brainstem reflexes, EEG classification (higher with suppression/burst suppression, alph-theta coma pattern, and epileptiform activity than with slowing of frequencies into theta or delta range), and EEG reactivity (higher with no reactivity).

The addition of clinical neurological and EEG evaluations to existing classification systems may help to better define prognostic strata in ICUs.

P109.

Hypoxic EEG Changes Induced by Tilt Table Testing

M.C. YEUNG, W.F. MURPHY and R.S. SHELDON (Calgary, Alberta)

Syncope results from a sudden impairment of brain metabolism usually brought about by hypotension with resultant reduction of cerebral blood flow. The purpose of this study was to determine if specific electroencephalographic changes could be identified in patients with syncope, and correlate these changes with clinical symptomatology.

Syncopal episodes were induced by isoproterenol-head-up tilt-table testing in 20 patients (12 females, 8 males, mean age 30 ± 19, median 5 syncopal episodes) who had continuous EEG monitoring. Nineteen patients had abnormal EEG's. One patient had theta waves, 2 patients had delta waves, and 2 patients had background suppression only. The remaining 14 patients had combinations of abnormalities. The most commonly seen progression was theta to delta to background suppression. The duration of abnormal EEG findings was 12 - 137 seconds. All patients regained consciousness within <30 seconds of the onset of syncope. Conclusions: (1) isoproterenol-head-up tilt-table testing can induce syncope, (2) EEG abnormalities during syncope are diffuse and correlate with previously recognized changes due to cerebral hypoxia, (3) no clinical or electroencephalographic epileptiform activity was seen, (4) only 1 patient had tonic posturing during testing; the remainder were flaccid, and (5) a normal EEG was rare in syncope.

P110.

Telephone Transmission of EEG: Appraisal of the Recordings

A. OGUNYEMI, J. GOODWIN, R. ARTS, A. HOPKINS and D. ADAMS (St. John's, Newfoundland)

The information available on the quality of EEG recordings obtained by telephone transmission is scanty. We have therefore investigated the quality and clinical utility of EEGs recorded via telephone transmission.

8-channel standard and telephone-transmitted EEGs were recorded simultaneously on 3 groups of patients: (1) 6 with normal neurological examinations and normal cranial CT scans (2) 8 with focal neurological deficits confirmed by CT scan of the head and (3) 8 with generalized or focal epileptiform abnormalities. The telephone EEGs were recorded after the signals had been transmitted via loops of telephone lines covering a distance of about 600 kilometres.

The EEG records were identified by codes and presented at random to two electroencephalographers for independent visual analysis and clinical interpretation. The 2 EEGs (standard and telephone) recorded simultaneously for each patient were then compared.

Specific attention was directed to the following features in the EEG tracings: (1) background activities such as alpha, mu and beta; (2) presence or absence of abnormalities such as epileptiform potentials and slow waves; (3) the quantity of artifacts, especially those related to telephone transmission, (4) alteration of recorded potentials, such as when muscle potentials simulated beta activities and vice versa. Other factors which degraded the quality of EEG records such as excessive baseline drift and interchannel crosstalk were also noted.

We observed that EEG tracings of acceptable quality can be recorded by telephone transmission. Limitations inherent in the technique and pitfalls in clinical interpretation will be discussed.

M. Epilepsy

P111.

Psychosocial Outcome of Temporal Lobectomy: Influence of Learned Helplessness

C.J. CHOVAZ, R.S. MCLACHLAN, P.A. DERRY, A.L. CUMMINGS, W.T. BLUME and J.P. GIRVIN (London, Ontario)

Learned helplessness is the perception that one's behaviour cannot produce a desired outcome. Individuals with intractable epilepsy who have learned that the occurrence of a seizure is beyond their control can develop a helpless attitude with cognitive affective and behavioural components which may generalize to many aspects of life. We hypothesized that the psychosocial outcome of temporal lobectomy is influenced negatively by learned helplessness independent of the degree of postoperative seizure control. Postoperative testing was done on 42 patients, aged 17-60 years with I.Q. > 80 who had temporal lobectomies (25 R, 17 L) with follow-up 1-14 years ($\bar{\chi}$ = 5 years). Seizure outcome was: completely seizure free since surgery, 36%; >90% improvement, 38%; <90% improvement, 26%. Three variables of learned helplessness were assessed: internal or external locus of control (Personal Reaction

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Inventory), resourcefulness (Self-Control Schedule), and depression (Beck Depression Inventory) as were psychosocial (Washington Psychosocial Seizure Inventory) and seizure outcome. Postoperative psychosocial adjustment was good as assessed both by the objective WPSI and subjective responses during a structured interview. Marked improvement in lifestyle was noted by 60%, personality change for the better by 57% and improved mood by 41% although a transient moderate to severe mood disorder was noted by 33% in the first 6 months following surgery. Psychosocial adjustment was better in patients who had >90% reduction in seizures or were seizure free than in those with <90% improvement. Two measures of learned helplessness, depression and lack of resourcefulness correlated with poor psychosocial adjustment independent of seizure outcome. The results of this study suggest that other variables besides seizure control must be considered in determining the ultimate outcome of epilepsy surgery.

P112.

Experimental Phenomenon from the Temporal Neocortex

W.T. BLUME (London, Ontario)

The relative roles which the temporal neocortex and the limbic system play in generating ictal experiential phenomena remain ambiguous. This case report clarifies the issue somewhat.

At age 18 years complex partial seizures began consisting of loss of awareness, lip smacking and automatisms. Fifty percent of these were heralded by a sensation in which everything would "slow down", including the speed of movement of objects in his environment, voices, and thinking processes. Removal of a left mid-posterior temporal neocortical malignant glioma abolished this experiential-type aura. Concern about memory caused the hippocampus and amygdala to be spared. For 2-3 years postoperatively attacks beginning with a diffuse cephalic sensation and nausea would occur. Subsequently they were replaced by an ascending abdominal sensation, sweating, dysphasia, and a vibrating shaking feeling of his right arm. As repeat carotid amytal tests reveal intact right temporal memory structures, the left amygdala and hippocampus were removed in 1988, 10 years after the initial operation. He has been seizure-free in the two postoperative years.

The abolition of his most common experiential phenomenon after the initial neocortical removal indicates that, while limbic structures may be necessary for experiential phenomena, participation of neocortical structures is also required for their occurrence.

P113.

Structural Studies On Endogenous Peptides Related To The Pathophysiology of Seizures

T. SCHEFTER, K. POTTER, K. O'CALLAGHAN and D. WEAVER (Kingston, Ontario)

An approach to the investigation of seizures arises from a study of the various endogenous factors that may ameliorate and suppress seizures. Numerous "endogenous anticonvulsant substances" including amino acids, peptides, prostaglandins, steroids, indoleamines and purines have been suggested. This study focuses on a group of peptides with antiepileptic activity.

Five peptides have been selected for study: thyrotropin releasing hormone, CCK-8, caerulein, FMRFamide and AAP (AAP is a recently described hexapeptide which supposedly blocks Ca++ channels thereby suppressing electrically excitable tissues.) The structures of these peptides have been ascertained using experimental and calculational techniques. Experimental conformational analysis was performed using nuclear magnetic resonance spectroscopy. Calculational conformational analysis was performed using molecular mechanics and molecular dynamics computational simulation. The conformational space has been explored rigorously using Monte Carlo search methods. A consideration of solvation (hydration) effects has been included.

Using these techniques, the structures of these five antiepileptic peptides have been studied. Correlations between structure and activity have been deduced. The importance of the geometric relationship between phenyl groups and amide nitrogen atoms within these peptides has been demonstrated. These results are applied to the identification of other peptides with putative antiepileptic activity and to an understanding of the molecular basis of seizure suppression.

P114.

Use of Evoked Potentials and Magnetic Resonance Imaging to Detect Vigabatrin Induced Brain Abnormalities in Dogs

N.M. SUSSMAN, C.E. SCHROEDER, K.L.WEISS, J.C. AREZZO, W.E. HEYDORN, J.P. GIBSON and R.G. MCBRIDE (Bronx; Cincinnati, U.S.A.)

Vigabatrin (Gamma vinyl GABA) is an irreversible inhibitor of GABA transaminase and is marketed in Europe as the antiepilepsy drug Sabril. In dogs, chronic vigabatrin administration produces reversible microvacuolation (intramyelinic edema) in discrete brain regions including fornix, hypothalamus, optic tracts and thalamus. A previous study (Arezzo et al. 1989) reports slowing in the central transmission portion of somatosensory evoked potentials (SEP) with chronic vigabatrin administration. The current study had three goals: 1) to replicate the earlier SEP findings, 2) to evaluate the sensitivity of visual evoked potentials (VEP), 3) to determine if structural changes could be visualized by magnetic resonance imaging (MRI).

SEP, VEP and MRI were assessed in 12 dogs prior to dosing. 8 dogs were randomized to receive 300 mg/kg/day of vigabatrin for 15 weeks and 4 to receive placebo. One treatment dog died at 2 weeks. Vigabatrin significantly increased the central transmission time of the SEP and absolute cortical latency of the VEP at 8 and 10 weeks respectively. There were no changes in peripheral nerve or spinal conduction. Both SEP and VEP measures returned to baseline within 5 weeks of stopping vigabatrin.

MRI were obtained with T1 and T2 weighting in coronal sections using a 1.5 Tesla GE Signa Magnet and a GE extremity coil. At 15 weeks all vigabatrin treated dogs showed increased T2 and decreased T1 signals in and surrounding the columns of the fornix and in discrete regions throughout the thalamus and hypothalamus. At 12 weeks after drug withdrawal, the MRI was markedly improved. Placebo treated dogs had no change in SEP, VEP or MRI. These data confirm the sensitivity of evoked potentials and MRI to vigabatrin induced microvacuolation in dogs and suggest the value of these measures in monitoring clinical populations treated with this compound.

P115.

"Acquired Epileptic Aphasia and Electrographic Status Epilepticus of Sleep: Two Sides of a Coin?"

A. HUNJAN, W. CHANG and P.A. HWANG (Toronto, Ontario)

At the Hospital for Sick Children, we have studied six children, three with acquired epileptic aphasia (Landau-Kleffner Syndrome)

and three with Electrographic Status Epilepticus of Sleep (ESES). There were 5 boys and 1 girl, aged 3 to 15 years. All showed speech deficit at 3 to 12 years of age, and 5 of 6 had seizures, 3 responded to anticonvulsants to some degree, but 1 required Prednisone.

All had waking and sleep EEG studies. The background activity was abnormal. All had focal epileptiform discharges in one or both hemispheres, particularly in the temporal regions. During sleep, generalized irregular spike-waves were recorded almost continuously, consistent with ESES.

We propose that the syndrome of acquired epileptic aphasia overlaps with the ESES syndrome, at least in a proportion of the cases studied.

P116.

Cognitive Deficits in Benign Childhood Epilepsy with Occipital Paroxysms (BCEOP)

K.J. GOULDEN, J. MAHER, T.B. GILBERT and G.M. RONEN (St. John's, Newfoundland)

In order to determine the frequency and type of specific cognitive deficit in BCEOP, children with this clinical and EEG-defined epileptic syndrome were prospectively studied. The study population was derived from the only pediatric EEG facility in the only tertiary-referral children's hospital in Newfoundland & Labrador. A history, physical examination and psychologic test battery were obtained on all children identified with the syndrome by review of EEG records, actual tracings, and then medical records. Fifteen children were found with recurrent unprovoked seizures associated with paroxysmal occipital EEG discharges and no other neurologic abnormality (i.e. uncomplicated BCEOP). All families consented to participate.

The 11 males/4 females ranged in age from 5-16 years (median 8 years). Only 2 were actively having seizures at the time of testing: one with <1 sz/mo and another with daily seizures despite 2 anticonvulsant drugs (AED). Eight others were on AED monotherapy; no child had toxic AED levels on the day of testing. Migraine was diagnosable in 10 children and another 4 had a family history of this. Eight (53%) had a family history of seizures.

One child was not yet in school (and was untestable because of short attention span/high activity level). School reports indicated the prior recognition of a need for special education services in 7/14 (50%). All children were of normal intelligence (mean IQ 92 ± 10). Thirteen of 14 (93%) had a significant dissociation between WISC-R indices [verbal comprehension, perceptual organization and freedom from distractibility]. School reports on all children agreed with the strengths and weaknesses found on testing. Only 2 children had any weakness in visual perceptual skills, which is quite surprising for any group with learning disabilities but particularly given the occipital lobe focus of this syndrome.

BCEOP is an epilepsy syndrome with a good prognosis for seizure control/remission. However, this "benign" epilepsy is associated with a very high risk of specific cognitive deficit or learning disability, which may have a significant and long-lasting effect on function.

P117.

Startle-Induced Myoclonic Seizures of Infancy - A Benign Epileptic Syndrome

R.I. MUNN, K. FARRELL, P.K.H. WONG and J.E. JAN (Vancouver, British Columbia)

Startle-induced seizures are rare in neurologically normal children. We describe four normal infants who developed startle induced myoclonic seizures.

Four boys, between 8 and 13 months of age, developed an abnormal startle response which was triggered by a sudden loud noise. Three infants had rhythmic, rapid jerks of both arms. The fourth had jerks of the head and neck. The episodes lasted 2-3 seconds and occurred 5-15 times per day. Past medical history, developmental milestones, family history and physical examination were unremarkable. Sudden, auditory stimuli precipitated myoclonic jerks which were accompanied by generalized bursts of atypical spike and wave on electroencephalogram. The episodes stopped spontaneously after two months in two infants and were controlled easily with valproic acid therapy in the other children. The medication was discontinued after one and two years respectively in the other children and they remain seizure free. One child has attention deficit disorder with hyperactivity.

The episodes occurred only when the infants were startled. The EEG confirmed that they represented seizures rather than a normal startle response. The similarity in the clinical and EEG features in these patients suggest that this constellation of findings may represent a syndrome of benign startle induced epilepsy in infancy.

P118.

De Novo Generalized Nonconvulsive Status Epilepticus in Older Adults: Evidence for a Secondarily Generalized Seizure Disorder

F. GRAND'MAISON, P. NAUD, S. GOSSELIN and J. REIHER (Sherbrooke, Quebec)

According to current prevailing views, generalized nonconvulsive status epilepticus (GNCS) occurring de novo in older patients belongs to the group of primary generalized seizures. Recorded observations in the literature of focal interictal and ictal abnormalities in some patients with GNCS are nevertheless intriguing. They prompted us to review our own material in all the patients aged 40 years and more with documented prolonged or repetitive nonconvulsive seizures associated with spike-wave complexes.

In 8 of 9 patients, aged 45 to 81, a unilateral, localized, temporal or extratemporal sustained rhythmic discharge signals seizure onset. Then follow bilateral generalized, initially asymetrical slow spike-wave discharges, and eventually more symetrical slow poly-spike and wave complexes. Attacks are rapidly interrupted by IV Benzodiazepines. Untreated discontinuous seizures are unusually prolonged, lasting an average of 11 minutes.

Failure to monitor in the majority of reported cases and in one of our 9 patients the focal initial events characteristic of a partial

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seizure disorder may explain the currently inappropriate classification of GNCS with the primary generalized seizure disorders.

P119.

An Unusual Form of Seizures Induced by Eye Closure

C.L. BARCLAY, M.A. LEE, H. DARWISH and W.F. MURPHY (Calgary, Alberta)

Seizures provoked by eye closure are a rare form of stimulus sensitive epilepsy. A review of the literature indicates that there are two forms of such seizures: those thought to be related to the absence of central visual input and those related to the movement of the eyelids. Both result in spike and wave discharges with are either isolated to the occipital regions or are maximal there. Both are said to have a good prognosis.

We present the case of a 19-year-old girl with an unusual form of epilepsy induced by eye closure. Her seizures began at age two with drop attacks and now include infrequent generalized tonic-clonic seizures and multiple daily events of rapid eyelid fluttering and an alteration of consciousness. The latter have not been altered by any form of drug therapy. Her EEG seizure pattern begins bifrontally and progresses to generalized high amplitude beta activity. This evolves into a periodic pattern of high amplitude beta alternating with slow activity. This periodic phase is associated clinically with eyelid fluttering. The ictal activity is terminated immediately on eye opening. By using passive eye closure, attempted eye closure against resistance, Frenzl lenses, eye opening and closure in the dark and focusing on a small red light in otherwise total darkness, it was determined that this girl has a type of scoto-sensitive epilepsy in which both the physical act of eye closure and the absence of visual input are necessary to provoke a seizure. No cases requiring both mechanisms have been described in the literature, although not all those reported underwent the above testing.

We conclude that this patient has a previously undescribed form of seizures and EEG seizure pattern provoked by eye closure in which both the physical movement of the eyelids and the lack of visual input are required to induce a seizure. The prognosis for seizure control in this type may be significantly worse than the previously described forms.

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P120.

Reading Related Cortical Potentials in Normal and Dyslexic Children

M.J. TAYLOR (Toronto, Ontario)

Event-related potentials (ERPs) are a sensitive means of assessing the timing and cortical utilization of cognitive processing. We have found ERPs to be valuable in the study of normal cognitive development, as well as in investigating cognitive disturbances, such as dyslexia. In the present series 32 children were studied; 16 normal controls and 16 dyslexic children. The dyslexic children were all of normal intelligence but at least one year below average reading ability. All showed primary deficits in auditory processing.

ERPs were recorded from a full head of 19 electrodes, with a bandpass of 1-30 Hz and a 1.5s sweep. Visual stimuli were presented via computer; subjects pressed a button to designated target stimuli. Three conditions were run: an orthographic task requiring children to judge whether the lower case letters had a closed loop (eg. a,p) a phonological task, requiring response to lower case letters that rhymed with "v", and a semantic task requiring response to animal words while ignoring other words. Target and nontarget stimuli were randomly interspersed, with targets occurring with a probability of 20%. The N2 and P3 peak latencies and the P3 amplitude (P3amp) were measured at all electrode sites for the three tasks. The data were submitted to repeated measures analyses of variance. P3 latencies decreased with age for all tasks and for N2 for the semantic and phonological tasks. P3 latencies were significantly longer in dyslexic children than control children, in the phonological and semantic tasks. In the simplest task, orthographic, no group differences were seen. In the phonological task (the only one requiring auditory processing) there was an age by group interaction; the P3 latency decreased in latency across age for the control children and not the dyslexic children. Across all three tasks, P3 amplitudes were largest at the parietal and occipital areas. The analysis of hemisphere effects revealed a trend with the P3amp in the orthographic task being higher in the right than left hemisphere, while the opposite was the case for the phonological and semantic tasks with higher P3amp in the left hemisphere. No significant differences in reaction time were found between the groups of ages, across the tasks.

The ERPs reflect the timing of information processing that varied with the task and population. The largest group differences were seen in the phonological task, reflecting the auditory processing deficits in the dyslexic children. The ERPs did not offer any suggestion of either a maturational delay or lag in cognitive development in the dyslexic children. The ERPs were more sensitive than the behavioural measures, for detecting the stage of information processing at which there is an impairment, and specifying the tasks that are more difficult in terms of cognitive processing for the dyslexic children. These data complement an earlier series of ours in which dyslexic children with visual processing deficits were studied.

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